

From the Ophthalmic Clinic of the University of Helsinki
Head: Professor Mauno Vannas, M. D.

1951

**STUDIES ON INTERSTITIAL KERATITIS
ASSOCIATED WITH CONGENITAL SYPHILIS
OCCURRING IN FINLAND**

BY

ARVO OKSALA

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Preface

This work was done in 1947—1950. The greater part of the material on which my studies are based was brought together and examined at the Ophthalmic Clinic of the University, Helsinki.

To *Mauno Vannas*, M.D., Professor of Ophthalmology, Head of the Ophthalmic Clinic of Helsinki University, I wish to express my deep-felt gratitude for his tireless interest and the support he gave in many forms, which made it possible for me to conclude the work which I began under his leadership.

Tauno Putkonen, M.D., University Lecturer, Chief of the Kumpula State Hospital for Venereal Diseases, Helsinki, gave me invaluable advice, without sparing his time or pains, especially in view of the venereological examination of my patients. He also allowed me to make use of the material of the hospital. For all this I am deeply grateful to him.

At the Ophthalmic Clinic of Turku University I was permitted to carry out investigations both in fresh and old cases. For this I am indebted to the Head of the Clinic at the time, Professor *Hilja Teräskeli*, M.D., as well as for valuable advice in the course of my work. I thank Doctor *Signe Löfgren*, M.Lic., Principal of Diakonissalaitos Hospital at Lahti and Doctor *Lauri Kiiänmies*, M.Lic., at Diakonissakoti Hospital, Oulu, for the material they made available to me and the opportunity allowed to carry out follow-up examinations at the Departments in question.

Many ophthalmologists have given me written and oral information of cases they had treated. Nurses and deaco-

nesses in different ophthalmic wards unselfishly helped me in my work. To all of them, without mentioning names, I wish to acknowledge my gratitude.

Lector Aune Tuomikoski, Mag. Phil., has translated this work in to English, for which I thank her in this connection.

Pori, August 1951.

Arvo Oksala

I. Some Important Achievements, up to the Present Date, of Studies on Interstitial Keratitis Associated with Congenital Syphilis

That syphilis may cause eye symptoms, was known as early as the 16th century, and there are records from the 17th century mentioning attempts to treat ocular symptoms of the disease with mercury, a medium still used for the purpose. Yet it was not until the 19th century that more scientific methods began to be applied in the study and treatment of diseases of the eye. In 1830 Lawrence, from England, published an investigation on ocular changes caused by venereal diseases, without mentioning, however, any disease resembling interstitial keratitis. Mackenzie, from England, described in 1840 a case of typical interstitial keratitis under the name »scrofulous keratitis». In 1851 the German Arlt used the name »keratitis interstitialis seu lymphatica» of typical interstitial keratitis without mentioning syphilis as an aetiological factor. The Englishman Wordsworth (1856) and the German Bader (1858) were the first to describe changes in the eye fundus due to congenital syphilis. But it was Jonathan Hutchinson, in 1863, who noted the causal connection between the condition nowadays called interstitial keratitis and congenital syphilis in his work »Clinical Memoir of Certain Diseases of the Eye and Ear Consequent on Inherited Syphilis», and considered congenital syphilis the sole cause of the disease. Hutchinson's groundbreaking ideas inspired a number of new investigations which not only met with acceptance but with fierce opposition (Panaset al.) as well. Hutchinson also described several so-

called congenital-syphilitic stigmas and signs, for example his own trias. He noted, besides, the occasional presence of joint symptoms in association with interstitial keratitis. Theobald Samuel (1871) was among the first who believed that acquired syphilis, as well, gave rise to a clinical picture similar to that of interstitial keratitis.

Arlt (1881) supposed that pure keratitis was rare in interstitial keratitis, since the uvea was usually involved contemporaneously, which view was accepted by many investigators at the time. Vossius described in 1885 a special form of the condition, calling it keratitis parenchymatosa annularis. Clutton brought out in 1886 his studies on temporary, usually bilateral and painless hydarthrosis occurring in connection with interstitial keratitis, later called »Clutton's joints». According to Alexander (1888), the disease usually began as a central opacity of the cornea, less often in the corneal margin. In his work »Syphilis», from 1888, Hutchinson mentioned that syphilitic iritis was more frequent in infants than was generally supposed. It often remained unidentified because of the slightness of the symptoms.

In 1895, Hirschberg described 6 different changes in the eye fundi of infants of 5—18 months affected with congenital syphilis. Haab, in 1898, classified the fundal changes caused by congenital syphilis into three different groups. Sidler-Huguenin, on the other hand, differentiated between four types of fundal changes in 1904, and his classification has remained the most common one. He considered keratitis and changes in the eye fundi mutually independent conditions. According to Igersheimer (1928), typical interstitial keratitis usually developed apart from the uvea, and the specific choroidal changes had usually preceded keratitis by several years.

A. Leber, in 1873, initiated experimental investigations on interstitial keratitis. By injuring the corneal endothelium of a non-syphilitic laboratory animal from the direction of the anterior chamber he produced haziness of the cornea, »Quellung», which soon disappeared. Hänsel (1881) was the first to demonstrate that syphilis may be

inoculated into the eye of a rabbit. *Wagenmann* carried out, in 1890, interesting experiments in which he caused in rabbits a clinical picture resembling interstitial keratitis by cutting off the long and short ciliary arteries.

The experimental investigations which *Bertarelli* started again in 1907 were the beginning of a series of others. When grafting tissue which contained spirochetes on the cornea of a rabbit he produced a disease picture similar to interstitial keratitis, noted an abundance of spirochetes in the cornea and demonstrated patho-anatomically the presence of lymphocytic infiltration around the vessels encircling the cornea. *Greef* and *Clausen* confirmed *Bertarelli's* results by injecting tissue from the inguinal lymph nodes which contained spirochetes, into the anterior chamber of a monkey and a rabbit, and by rubbing some of it, crushed, into a damaged cornea. Similar experiments were carried out on animals by for example *Scherber*, *Schacht* and *Schultze* about the same time. *A. Leber*, in 1906, obtained a clinical picture resembling interstitial keratitis by inoculating a species of trypanosoma into the anterior chamber of a dog and a rabbit. *Clausen* (1912) noted the disappearance, occasionally, of the spirochetes from the corneas of the laboratory animals after a time, even without any treatment. He found that no analogy could be established between this interstitial keratitis and the one in man, and used, like *E. Hoffmann*, the name »primary syphiloma of the cornea» of the keratitis brought about experimentally. *Clausen* did not observe any of the general symptoms consequent on the disease after keratitis produced experimentally. *Grüter* wrote in 1910—1911 that »Eine einfache Hautritzung mit der Impflanze wohl eine Immunität der gesamten Hautdecke, nicht aber der Hornhaut hervorruft».

The experiment carried out by *K. Wessely* in 1911 and later called the *Wessely phenomenon*, proved very significant for further experimental studies. 1—2 drops of sterile inactivated serum of the the ox or of the horse were injected into the rabbit's cornea, in which, following temporary irritation, a condition resembling interstitial keratitis

set in after about a fortnight. A. von Szily in his work »Anaphylaxie in der Augenheilkunde«, from 1914, reported on the experimental investigations he had performed together with Arisawa. They distinguished between 5 different types of anaphylaxia of the cornea pointing out that in their experiment the first sensitization might occur without any clinically observable symptoms. F. Schieck in his book »Die Immunitätsforschung im Dienste der Augenheilkunde«, from 1914, dealt with the phenomenon of anaphylaxia from the viewpoint of eye diseases and explained his own view, based on recognition of anaphylaxis, of the origin of interstitial keratitis. In his experimental studies Igersheimer noted spirochetes in the cornea at the edge of the lesion, as is usually the case in a primary syphilitic lesion, but none in the iris. He also found that there was some immunity against spirochetes in the eye. According to him, spirochetes inoculated into the anterior chamber penetrated into the cornea through the endothelium. He did not find that trauma played any part in experimental syphilitic keratitis, which moreover healed well with anti-syphilitic treatment. Cattaneo (1924) produced experimental keratitis by inoculating spirochetes under the conjunctiva, into the cornea and the anterior chamber. After subconjunctival inoculation he found spirochetes in the cornea. Histological examination revealed perivascular lymphocytic infiltration of the limbus. According to Cattaneo the spirochetes invaded the cornea from the direction of the anterior chamber and the limbus. After an inoculation into the anterior chamber he saw patches of chorioiditis in the eye. He did not find that any immunization took place in the experimental investigation.

A. Löwenstein (1927) made a study of the spontaneous keratitis occurring in syphilitic rabbits. Patho-anatomically he noted large tracts of infiltration around the scleral blood vessels of the animals studied, the smaller vessels especially seemed to be obstructed by round cell infiltrates. He noted perivascular infiltration in the deep vessels of the cornea as well. Clapp (1933) confirmed, furthermore, the findings of Bertarelli, Greef & Clau-

sen, Igersheimer and others when noting spirochetes in the cornea of rabbits with experimental keratitis both biologically and by staining, after subconjunctival inoculation of spirochetes. Yokota (1935) showed by experiments that the disorder spread in the cornea from the surface towards the depth, and he supposed that the spirochetes usually invaded the cornea from the direction of the limbus. He wrote in opposition to Igersheimer's concept: »Es is überhaupt schwer annehmbar, dass die Spirochäten von der Vorderkammer her durch die Deszement hindurch vordringen«. Chesney, Woods and Campbell (1939) studied on rabbits the development of immunity against spirochetes. They actually noted immunization in the cornea, though it was slight and often observable only with difficulty. On the skin, on the other hand, the process of immunization was much more marked. They did not notice any allergic symptom in the cornea nor did they find that their experiments supported Igersheimer's theory on the pathogenesis of interstitial keratitis, which I shall describe later.

Soon after Hutchinson's epoch-making findings it was realized that congenital syphilis alone could not account satisfactorily for the development of interstitial keratitis. In the following decades several different theories were brought forward on the origin of the disease, of which those that met with most favour arose from the recognition of an anaphylactic reaction. Yet none of the aetiological theories that will now be described have found universal acceptance nor have they been proved tenable on all points.

Wagenmann supposed on the basis of his experiments that the interstitial keratitis of man resulted from nutritional disturbances in the cornea, which view also found favour with others, e.g. v. Michel. Schultze (1896) considered that both syphilitic and tuberculous deep keratitis developed as a result of destruction of corneal endothelium. The endothelium was destroyed through nutritional disturbances, after which toxins of the aqueous humour invaded the corneal parenchyma. E. v. Hippel brought out a number of papers on the disease. In 1893

he wrote that there are a great many cases of primary type in which no syphilis can be demonstrated either subjectively or objectively, and that tuberculosis is a significant aetiological factor. In his view clinical primarity does not rule out actual secondarity, and he did not recognize any difference, in principle, between the two forms. In a case he studied patho-anatomically, v. Hippel noted changes in all parts of the eye, i.e. it was an instance of a kind of panophthalmitis. Yet he found himself unable to make any inferences as to the primary site of the disease from the changes he had noted, and declared that the condition was apparently due to endogenic factors. The infection or the toxins, he said, entered the eye by way of the ciliary arteries. Damage done to vascular walls might also result in nutritional disturbances.

Perlia (1905) was the first to emphasize the significance of trauma in the aetiology of interstitial keratitis. Holmes Spicer (1924) noted a connection between the disease and trauma in 3 % of his cases, likewise Carvill and Derby in 1925. Igersheimer (1928) expressed his doubts as to the possibility that the disease might have been caused by trauma.

Elschnig, in 1906, dealt extensively with the problem of interstitial keratitis and described at the same time a case he had examined patho-anatomically, in which he considered the primary change to have taken place in the cornea. Elschnig did not believe the disease would involve the cornea by way of the aqueous humour and the endothelium. He did not regard the disease as corneal syphilis in spite of its syphilitic origin but thought that it was, primarily, one of the degenerative changes of the cornea. He attributed the genesis of the disorder to anaphylactic reactions, declaring that some corneal or uveal trauma or disturbances in metabolism caused disintegration of the tissue, such as necrosing, which led to resorption of the protein specific to the ocular organs in question as an antigen into the general blood circulation. The proteins present in different organs, according to him, were not as such within the reach of antibodies but only as a result

of the new cause. A. L e b e r (1907—1910) was the first to examine patients with interstitial keratitis by the Wassermann and Pirquet tests, which then revealed syphilis in 83.9 %, and in 74 % of the cases in his second work. The ratio between acquired and congenital syphilis, according to him, was 11 : 63, approximately. K ü m m e l (1909) did not rank the tuberculin test very high as a diagnostic medium. C l a u s e n established, in 1912, 99.24 % as the share of syphilis in the aetiology of the disease, and the ratio between acquired and congenital syphilis roughly at 11 : 79. In spite of careful attempts, he found no spirochetes patho-anatomically in 14 corneas affected with interstitial keratitis. I g e r s h e i m e r's one finding could not assure him that the genesis of interstitial keratitis was bound up with the presence of the spirochete in the cornea. He believed that the disease was due to a general nutritional disturbance of the cornea, which was preceded by peri- and endovasculitis of the pericorneal vessels. He considered the findings obtained from the corneas of foeti and newborn infants who were affected with congenital syphilis (B a b 1906) of less significance. C l a u s e n assigned a larger share to acquired syphilis in the genesis of the disease than for instance I g e r s h e i m e r.

W e s s e l y, on the basis of the phenomenon called after him, explained the outbreak of the disease from the periodically varying hypersensitivity of the organism to spirochetes. K r a u p a (1912), in contrast to E l s c h n i g's view just described, concluded that the formation of antibodies against the cornea of the same species, though possible, was much more difficult than against foreign corneal tissue. S c h i e c k found the most vulnerable point in E l s c h n i g's theory in the fact that the organism usually develops antibodies to its own proteins with difficulty. Yet S c h i e c k found it probable that anaphylactic reactions had a share in the genesis of the disease, and stressed the fact that the cornea does not participate in metabolism to the same extent as other tissue of the body. Spirochetes had a passive share only in the disease. He supposed that the corneas of patients with

congenital syphilis contained an antigen of spirochetes from birth, which did not participate in the general metabolism of the body. While the whole organism produced antibodies against spirochetes, the cornea remained apart. When some cause such as trauma, infection etc. increased the metabolism of the cornea, antibodies found their way even to corneal tissue, giving rise to an anaphylactic reaction. v. Szily put forward theories to account for the development of the disease. According to one, the spirochetes cause the disintegration of corneal tissue, and the protein of the disintegrated tissue acts as a protein-antigen, foreign to the species, or, the cornea is sensitized by spirochetes, and the resulting inflammation is then a consequence of the reaction between the sensitized tissue and the antigens circulating in the blood.

According to Igersheimer's theory, which became accepted widely, the presence of spirochetes in the cornea is a necessary condition for the development of interstitial keratitis. As early as the foetal stage the cornea was sensitized by the metabolic products of spirochetes which had invaded it, which later gave rise to an anaphylactic reaction between the antigens carried there from some other part of the body and the metabolic products of spirochetes. Igersheimer declared that typical interstitial keratitis could be attributed to congenital syphilis in nearly 100 % of the cases. He wrote about the share of acquired syphilis: »Es ist nun zweifellos eine der merkwürdigsten Tatsachen der Ophthalmologie, dass eine an sich so häufige Erkrankung wie Keratitis parenchymatosa so oft bei kongenitaler und so selten bei akquirierter Lues vorkommt.« Tuberculosis apparently did not cause primary interstitial keratitis. Holmes Spicer understood the genesis of the disease thus that during the generalization the spirochetes invaded the cornea in anticipation of suitable conditions for new development and increase. The iris and the ciliary body could also be primarily affected. His series consisted of nearly 700 cases of which he considered 3.3 % due to acquired and 90 % to congenital syphilis. Guy (1926) agreed with Igersheimer in believing that the out-

break of the disease was connected with the presence of the spirochete in the cornea. When commenting on the pathology of the disease he wrote: »It would seem that in interstitial keratitis we are dealing with a gummatous type of process.» *Vogt*, in 1930, described in his textbook a case of interstitial keratitis which he had followed from the beginning. The first sign of the disease had been slight haziness of Descemet's membrane close by the limbus. In another case the disease began as a marked thickening of the limbus, which pointed to localization of the infiltrates in the sclera and not in the cornea.

Löwenstein, from his investigations, considered obstruction of the anterior ciliary vessels the actual cause of the outbreak of interstitial keratitis. Possible hypersensitivity of the tissue might occur as a result of impairment of the blood circulation and the metabolism, in which case the disintegrated corneal protein would act as an antigen. He could not accept *Igersheimer's* view about the spirochete having a direct share in the genesis of the disease.

Nor did *Seefeldter* (1933) believe in a direct effect of the spirochete. He pointed out the fact that the patho-anatomical picture was not typical of syphilitic inflammation. *Seefeldter* noted that the disease was always accompanied by iritis, which was also *Cattaneo's* opinion. *de Sanctis* (1936) declared that the corneal changes were without exception preceded by inflammation of the iris and the ciliary body.

Behr (1936) brought forward a new modification of the theories on the aetiology of interstitial keratitis. He did not think that the disease was directly caused by a spirochete but wrote: »Sie (keratitis parenchymatosa) steht also in Parallele zu der Metalues mit dem Unterschied, dass hier das mesodermale Gewebe nach der Formel Spirochäten + parasymphilitisches Prinzip + organ (Cornea) reagiert, ferner dass eine fötale Infektion Vorbedingung ist.» The outbreak of the disease was thus conditioned by some kind of change in the reactional condition of the body. *Granström* (1937) supposed that the disease would only set in if in-

fection, intra- or extrauterine, took place before the termination of the developmental age. The author noted no differences in the clinical pictures of young and older patients. Johnson and Eckhardt (1940) supposed that ariboflavinosis had some share in the new vascularization in the cornea of patients with interstitial keratitis. Grütter's (1949) view of the aetiology of the disease was that the actual outbreak of keratitis due to some virus and that the part played by congenital syphilis was only of a predisposing nature.

Enroth (1920), from Finland, was among the first who made a thorough study of the share of constitutional and endocrine factors in the genesis of interstitial keratitis. Enroth did not believe that the spirochete actually brought about the disease, but declared: »Dass bei dem Zustandekommen der Hornhauterkrankung in erster Reihe eine konstitutionelle Krankheitsbereitschaft unerlässlich wäre». Primarily interstitial keratitis would thus be a degenerative disease. Enroth and Hisinger-Jägerskiöld (1925) almost regularly noted, in cases of interstitial keratitis, a pathological picture of the skin capillaries which they considered not a syphilitic symptom but a sign indicative of an abnormal constitution. Kraupa (1921) suggested that a neuropathic constitution might be of some significance in the development of the disease. According to Gange and Antoine (1925) the share of endocrine factors in the outbreak of interstitial keratitis was to be taken into account for the following reasons: (1) these patients often exhibit endocrine disturbances, (2) the disease usually breaks out in puberty and is more common in women, (3) hormonal therapy, according to these authors, has given good results, and (4) opacity of the corneal parenchyma has often been produced in laboratory animals by removing endocrine glands. Towbin and Prorowsky (1929) noted pathological changes in the vegetative-endocrine systems in nearly all of their 20 patients with interstitial keratitis. Thyroidal changes were the most manifest. Prokopenko (1930) also presumed that functional disturbances of the endocrine glands had some

share in the genesis of the disease. Similar views were put forward by T e r r i e n (1933) and others. I g e r s h e i m e r wrote that congenital syphilis predisposed the patient to various diseased conditions such as tuberculosis, rachitis and endocrine disturbances. A j o (1946) noted changes in basic metabolism during antiluetic treatment.

A. v. G r a e f e embraced in his time the view which many authors find tenable even today that all treatment of interstitial keratitis is comparatively ineffective as far as the keratitis itself is concerned and that the physician is more or less just a »looker-on». Besides antisyphilitic treatment, many other methods of most various kinds have been tried, but they have always before long been superseded by ordinary local treatment of the eye. There have always been greatly differing views about the efficacy of antisyphilitic treatment. Since I intend to review the opinions of different authors later in connection with my own studies, I only mention them briefly here. — Soon after the invention of salvarsan C l a u s e n and many other ophthalmologists declared that it had no appreciable effect on the course of the disease. The manifest effectiveness of antiluetic treatment (arsenic + heavy metal) in interstitial keratitis was believed in by C a r v i l l & D e r b y, L a n g e n d o r f f, W e v e, and K l a u d e r & V a n d o r e n et al. H o l m e s S p i c e r, I g e r s h e i m e r, S e e f e l d e r, and H o e h n e were among those who in many cases took a doubtful and partly even negative view of the good results obtained by antisyphilitic treatment. K o p p and S o l o m o n (1940) declared that non-specific fever therapy given in the neurosyphilis of patients with congenital syphilis could predispose them to keratitis by activating slight chronic inflammation. K l a u d e r (1947) considered penicillin a similar step forward in the treatment of the disease as salvarsan had been when first introduced. Results equal to those achieved by arsenic + bismuth treatment were obtained with penicillin by for example F o r s y t h, G r a h a m, R o m a i n e, and R u l i s o n and I n g r a h a m.

One still finds very variable views on the importance

of cortisone and ACTH in the treatment of interstitial keratitis. Woods¹⁾ (1950) with systemic ACTH therapy and Leopold, Purnell et collab. with local cortisone therapy noticed no improvement in their cases, while e.g. Salomaa & Swanljung mention that cortisone and ACTH affected the course of the disease favourably. Franceschetti & Maeder and Thiel found local cortisone therapy beneficial. The series reported on are still small and times of observation short.

Notice was paid quite early to the social significance of syphilitic eye diseases. Alexander claimed as early as 1888 in his large monograph that 2.76 % of all diseases of the eye were syphilitic. According to Ohanian (1920) about 0.5 % of all eye diseases in America (29 528 cases) were caused by congenital syphilis. Sinclair (1922) had noted interstitial keratitis in over 1 % of 10054 British eye patients. Holmes Spicer, likewise in Britain, declared that 0.6 % of eye patients were affected with interstitial keratitis. Guy (1926), on the other hand, met with interstitial keratitis in about 1 % of 15 000 patients with eye diseases, in America. — Widmark, in 1902, pointed out the considerable share of venereal diseases in causing blindness. According to him, in 20 % of cases in the Scandinavian countries, blindness was due to these diseases, and in 14—15 % to syphilis specifically. Bishop Harman (1921), in Britain, attributed 9.19 % of 925 cases of partial or total blindness to syphilis and about 3 % to interstitial keratitis. He considered syphilis the most important and greatest of the preventable causes of blindness. Lawsøn (1922) estimated, likewise in Britain, the share of syphilis as a cause of blindness at 10—15 %. — Green (1920) had noted the presence of interstitial keratitis in about 50 % of patients with late congenital syphilis. Cannon (1927) considered interstitial keratitis the commonest symptom of congenital syphilis, and estimated its incidence

1) Woods, however, stated recently (1951): The stage of the disease, when the treatment is started and the method of treatment profoundly influence the result. The earlier treatment is started, the better the results and topical application of cortisone appears superior to the parenteral administration of either cortisone or ACTH.»

at 35 %. Smith (1927) examined 1000 patients with congenital syphilis, of whom 641 had been affected with interstitial keratitis. Cole, Usilton, Moore et collab. noted in 1937 that interstitial keratitis occurred in 39.9 % of 1010 congenital syphilis patients. Klauder and Cowan (1939) obtained 25—50 as the corresponding percentage. They mentioned at the same time 0.5—3 as the approximate percentage of the incidence of congenital syphilis among the American population.

A great number of analytic studies on interstitial keratitis based on both small and larger materials were published in 1920—1940. These studies dealt with various aspects of the disease and they have contributed materially to our knowledge of it. Derby (1917) was among the first to make a thorough study of the deterioration of vision caused by the disease, and he has been followed by a number of investigators such as Langendorff, Carvill & Derby, Smith, Igersheimer, Schweickhardt, Dalsgaard-Nielsen and Klauder & Vandoren. In their large work Carvill and Derby compared the results obtained on patients treated specifically and those that were not treated, which study was among the first of its kind. The social-hygienic problems caused by the disease especially in view of vision were given attention to by Carvill & Derby, Schweickhardt and Dalsgaard-Nielsen, and others. Many of these analytic studies will be dealt with in more detail later, in connection with my own investigations.

Hirschberg and v. Hippel, in the past century, paid especial notice to the so-called deep blood vessels of the corneal parenchyma and considered their formation a lasting and persistive change. Kleefeld, among others, took the same view in the paper he published in 1924. Swindle (1938) studied corneal vascularization on different species of animals. He saw vessels being formed from anastomoses of the vascular system of the limbus. The limbal vessels had dilated at the same time, and small hemorrhage were seen nearby. The author found the dilated arteriovenous anastomoses facilitated the entrance of the

new vessels between the corneal lamellae. C o g a n (1949) studied experimentally vascularization in the cornea, of which the first discernible sign was aneyrism in the nearest limbal vessel, followed by small haemorrhage and formation of new capillaries. The new vascularization was always preceded by thickening of the stroma and increasing opacity of its tissue. C o g a n considered the reduced consistency and resistance of the corneal stroma an essential factor. O f f r e t and C h a u v e t (1950) emphasized, besides, the share of respiratory failures and avitaminosis, especially ariboflavinosis, in the formation of deep blood vessels.

S t ä h l i published in 1919 3 cases in which he had noted so-called hyaline striae on the posterior surface of the cornea several years after interstitial keratitis. Identical formations have since then been met with and studied by several other authors, for example W e i l & J o s t, K e s t e n b a u m, V o g t and B e r l i n e r.

Besides by the authors mentioned in the foregoing, patho-anatomical studies have been brought out by S t a n - c u l e a n o, W a t a n a b e, K u n z e, J a e g e r, S e e - f e l d e r, M e y e r, B e n t e l e and W e s k a m p, and others. None of them had found spirochetes in the cornea. Only I g e r s h e i m e r and W e v e had noted spirochetes in the corneas of patients who had become affected at an age usual for the onset of the disease. J. S. F r i e d e n - w a l d published in 1930 his interesting studies on the eyes of infants affected with congenital syphilis. In these patho-anatomical studies he found inflammatory changes in the eyes of 9 patients out of 30. Spirochetes were revealed especially in the sheaths of the blood vessels perforating the sclera and the uvea. Changes occurred in irides and ciliary bodies of 5 eyes.

II. Own Investigations

Purpose and Plan of the Work

Different aspects of interstitial keratitis associated with congenital syphilis have been dealt with in a great number of studies published in the course of nearly a hundred years. Yet the disease still remains an important and interesting problem. Although considerable progress has been made in the treatment of both acquired and congenital syphilis in the present century, much still remains to be done as far as the results of the treatment of the interstitial keratitis which occurs in association with congenital syphilis are concerned. The preventative treatment of congenital syphilis and interstitial keratitis, a question which is very important both from the medical and the social viewpoint, has thus received increasing attention.

International co-operation has helped to promote research for the prevention and treatment of syphilis and particularly congenital syphilis, and the share of penicillin, which has proved a rapid and effective medium with a view of this disease as well, is worthy of especial mention. However, for effective international work it is important that the part played by the disease in question among the populations of each country should be thoroughly elucidated. Since interstitial keratitis gives a fairly reliable picture, although a small-scale one, of the total problem of congenital syphilis, and since the significance of this important and not uncommon disease has not yet been dealt with in Finland, I have undertaken this work.

To obtain some kind of picture of the frequency of the disease in Finland I have brought together the cases of in-

terstitial keratitis associated with congenital syphilis revealed in Finland in 1922—1950, availing myself of the files of various hospitals and inquiries addressed to ophthalmologists. To establish the ultimate vision of each patient as accurately as possible I carried out follow-up examinations personally and undertook them only in those cases where at least 1 year had elapsed from the termination of the active phase of the disease. The follow-ups were carried out in 1947—1950 in several localities, namely at the University Ophthalmic Clinic in Helsinki, at the University Ophthalmic Clinic in Turku, at the Ophthalmic Department of Diakonissakoti Hospital at Oulu and at the Ophthalmic Department of Diakonissalaitos Hospital at Lahti.

In the follow-ups I estimated the vision of the patients and examined their corneas, scleras, irides, lenses and chamber angles with the slit lamp. I paid notice to changes in the eye fundus and the sensitivity of the cornea. As far as possible I examined my patients from the venereological aspect as well. I also tried to find out about the social background of these patients who were »guiltless» of their affliction. I entered, besides, into many central problems of the study of interstitial keratitis associated with congenital syphilis in the light of my own material.

III. Material

1. *Classification*

The material which I have dealt with in my work divides itself into 2 groups: (1) The new cases of interstitial keratitis associated with congenital syphilis revealed in the whole country in 1922—1950, and (2) the patients who came to my own follow-ups.

I brought together the first group of my material, consisting of 731 patients, from new cases of interstitial keratitis associated with congenital syphilis registered at different hospitals. They distribute themselves among the hospitals as follows:

The Ophthalmic Clinic of the University, Helsinki, 1922—1950, 451 cases,
the Ophthalmic Clinic of the University, Turku, 1938—1950, 52 cases,
the Ophthalmic Department of Diakonissakoti Hospital, Oulu, 1932—1950, 110 cases,
the Ophthalmic Department of Diakonissalaitos Hospital, Lahti, 1940—1950, 36 cases,
the Ophthalmic Department of Kivelä Hospital, Helsinki, 1937—1950, 21 cases,
the Provincial Hospital of Kuopio, 1940—1950, 31 cases,
the Ophthalmic Department of the Provincial Hospital of Vaasa, 1941—1950, 18 cases,
Kumpula State Hospital for Venereal Diseases, Helsinki, 1945—1950, 12 cases.

Of these patients about 500 were invited by letter to follow-up examinations. In spite of many difficulties such as changes of address and deaths that had occurred in the

course of about 30 years, long distances, special circumstances caused by two wars, etc., 128 patients turned up for late examinations. They distribute themselves among the different hospitals as follows:

The Ophthalmic Clinic of the University, Helsinki, 39 patients,
 the Ophthalmic Clinic of the University, Turku, 26 » ,
 the Ophthalmic Department of Diakonissakoti Hospital,
 Oulu, 35 patients,
 the Ophthalmic Department of Diakonissalaitos Hospital,
 Lahti, 16 patients,
 the Ophthalmic Department of Kivelä Hospital, Helsinki,
 6 patients and
 Kumpula State Hospital for Venereal Diseases, Helsinki,
 6 patients.

2. Incidence of the Disease in Finland

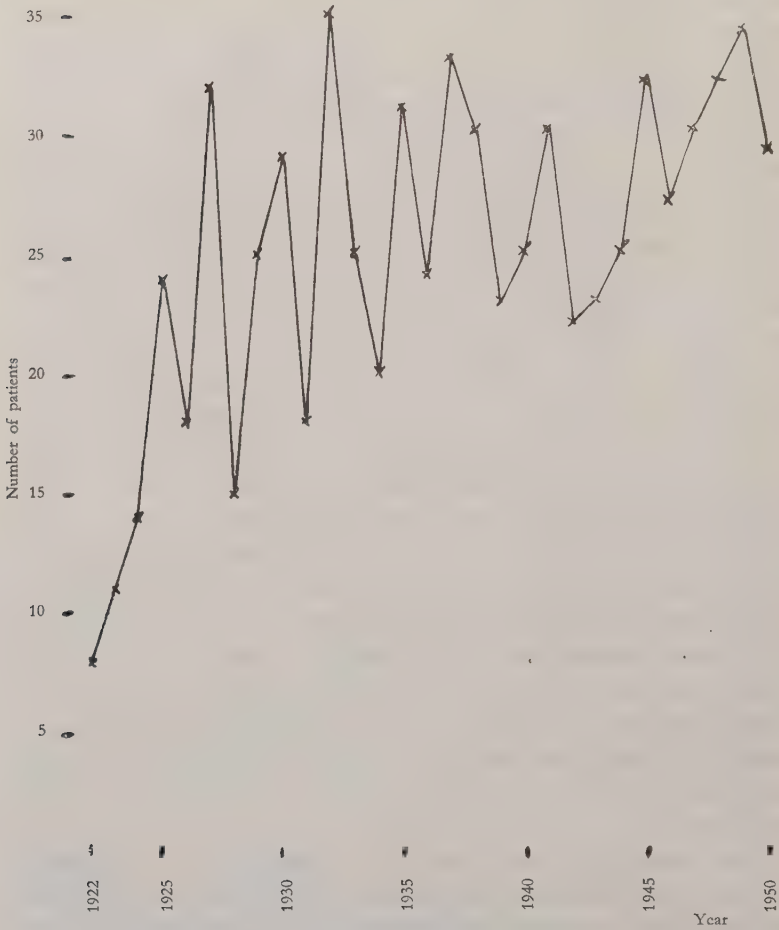
Most of the cases of interstitial keratitis associated with congenital syphilis are of a kind for which patients as a rule go to an ophthalmologist or an Eye Department for treatment. But in Finland, where there have always been few ophthalmologists in the provinces, a many of these patients have to manage without a specialist's help and are then often given treatment indicated by most various diagnoses. In mild cases the patients probably do not seek medical help at all. It is not unlikely that in 1940—1945, in many cases, war-time circumstances made appropriate treatment at a special department impracticable. In spite of these factors and many others leading to inaccuracy I considered it worth while to collect all the cases of interstitial keratitis treated at our various Eye Hospitals, for there is no doubt, I think, that the bulk of the patients in this country fall under this group. Unfortunately the records of the Ophthalmic Department of Diakonissalaitos Hospital at Viipuri disappeared in war-time conditions, among them the case histories of about ten patients to every year.¹⁾

¹⁾ For this estimate I am indebted to Doctor Signe Löfgren, who was in of the Department for over ten years.

The bulk of my entire material, self-evidently, comes from the Ophthalmic Clinic of Helsinki University, and consists of patients treated there in 1922—1950. I have estimated that by 1922 the unsettled conditions due to the War of Independence had become relatively stabilized. In the 1920's the Ophthalmic Department of Diakonissalaitos Hospital at Viipuri was the only hospital of its kind in the provinces. Beginning with 1932 I included among my material the patients of the Ophthalmic Department of Diakonissakoti Hospital at Oulu and since 1937 those of the Ophthalmic Department of Kivelä Hospital, one of the municipal hospitals of Helsinki, and since 1938 the patients of the Provincial Hospital of Turku (Ophthalmic Clinic of Turku University). Since 1940 I have taken into account cases from the Ophthalmic Departments of Diakonissalaitos Hospital at Lahti and the Provincial Hospital of Kuopio, since 1941 from the Ophthalmic Department of the Provincial Hospital of Vaasa and since 1945 those from the Kumpula State Hospital for Venereal Diseases, Helsinki. The contingent of the patients treated at the Ophthalmic Clinic of Helsinki University has thus diminished gradually, so that the statistics from this hospital alone do not suffice for an estimation of the incidence of the disease in the whole country. The curve in the following Fig. 1. p. 26 records the yearly number of new cases of interstitial keratitis associated with congenital syphilis treated at the various Hospitals.

It is obvious from what I have said in the foregoing that at least the cases treated at the Ophthalmic Department of Diakonissalaitos Hospital at Viipuri would have been required to supplement the figures recorded for the years before 1940. Yet this information is no longer available. It is partly because of this, apparently, that the curve shows surprisingly great fluctuation in the 1920's and at the beginning of the 1930's, when this Department was the only one of its kind in the provinces. In his papers from 1948 and 1950 dealing with the incidence of primary and secondary syphilis in Finland in 1923—1950, P u t k o n e n noted considerable fluctuation in the curve he drew

Fig. 1. Incidence of interstitial keratitis associated with congenital syphilis in Finland in 1922—1950.



to illustrate the incidence of the disease. Putkonen's curve ran very low in 1937—1940. My curve, which is possibly affected by the consequences of the wars, does not show at any corresponding fall, which from the estimates I made of the age when the disease appeared in each case, ought to have followed after about 7—10 years.

To sum up, it might be said that *the disease showed no tendency of decline in 1922—1939 in Finland (with the exclusion of Eastern Finland) and in 1940—1950 in the whole of the*

country. It is somewhat presumptuous, in the absence of information from Eastern Finland, to attempt an estimate of the possible difference between the two periods, but I would say that no radical change can have taken place on this point.

One might of course assume that the growing number of ophthalmologists and Ophthalmic Departments in the provinces would in itself increase the number of the cases diagnosed in the last twenty years. On the other hand, the clinical picture of interstitial keratitis is in the majority of cases so unmistakable and the disease so protracted and severe that even in the earliest years the patients have usually, as far as possible, been taken to a specialist for treatment. The increase in the population, on the other hand, has not been so great that it could change my view about the incidence of the disease in 1922—1950 presented in the foregoing.

It is of course extremely difficult to estimate the number of the patients living at present in this country, who suffer from interstitial keratitis associated with congenital syphilis. My own material affords some kind of basis, though an inaccurate one, for such an estimation. Therefore I cannot avoid the temptation to bring out my estimate, since the result, in spite of its inaccuracy, is not lacking in interest and possibly even significance.

At the University Ophthalmic Clinic in Helsinki a total of 451 fresh cases of the disease were treated in 1922—1950, 20.4 % of them as out-patients. The total number of fresh cases at the other Eye Departments was 280 in the years 1932—1950, which figure includes also the fresh cases admitted at the Kumpula State Hospital for Venereal Diseases. The figures for 1922—1939 ought to be supplemented by the cases treated at Diakonissalaitos Hospital at Viipuri, estimated to total about 160—170. Some private practitioners have treated a few cases polyclinically, besides, whose number, according to answers to personal inquiries and a comparison with the cases treated at the Ophthalmic Clinic of Helsinki University can hardly have been more than 6 patients yearly. The number of patients

within these years, who did not present themselves for treatment, would be about 60 according to an estimate based on my own investigations (see p. 63). The fresh cases of interstitial keratitis in the whole country would thus total roughly 1100 for 1922—1950. If we reckon that the average lifetime of these patients is what several authors and myself have estimated as approximately normal, the number of cases in the whole country would at the moment be about 2000—2200.

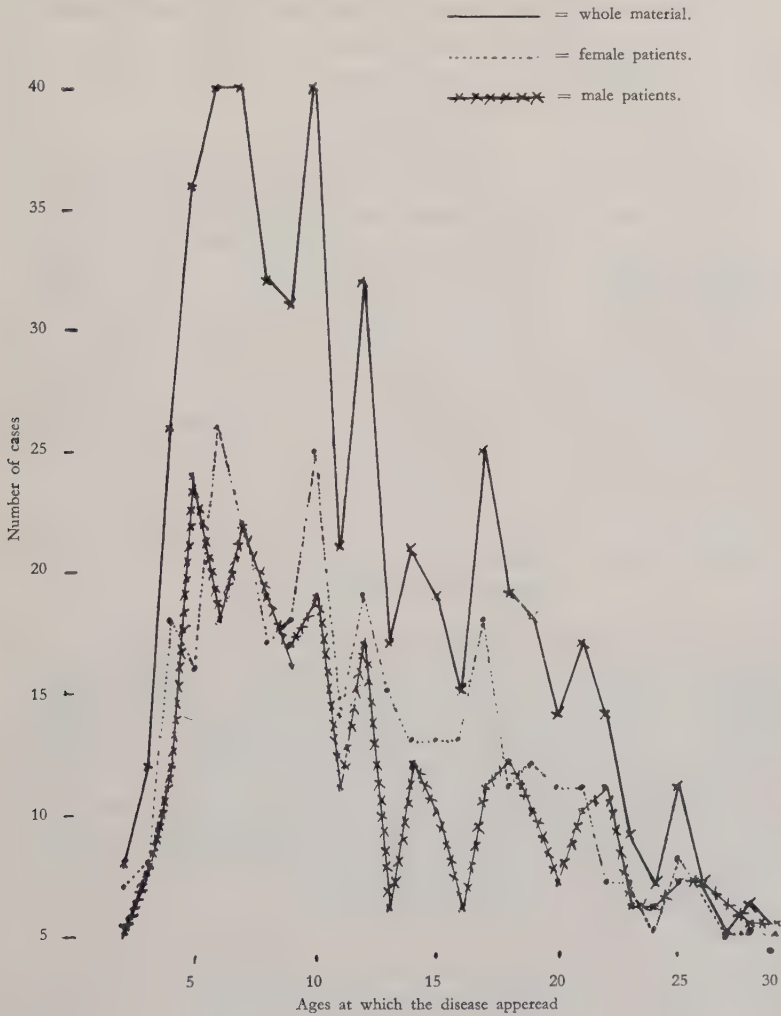
That the disease will continue to be fairly common in Finland for quite a number of years is evident from the sharp increase of cases of primary and secondary syphilis in 1942—1945 demonstrated by P u t k o n e n's studies. On the other hand it may be expected that the extensive and vigorous work to combat syphilis which has been going on in this country for some years and of the results of which, according to P u t k o n e n, the statistics for 1948 bear evidence, will later on definitely reduce the number of the cases of interstitial keratitis associated with congenital syphilis.

3. Age of the Patients at the Onset of the Disease

I made notes of the patients' age at the time of the onset of the disease in the 451 cases treated at the Ophthalmic Clinic of Helsinki University. For further study I drew up a Figure in which the number of the patients of the whole material and that of the male and female patients separately were entered against each year of age (Fig. 2, p. 29).

According to the Figure the commonest age for the disease to set in was between 4 and 12 years, approximately, in 58 % of the total number of cases. Both the male and female patients usually developed the disease between these years. The disease also fairly frequently appears between 13 and 22 years of age, in about 31 % of the patients in the material. After 23 one meets the disease less often. *It may be said that the disease appears about twice as often between*

Fig. 2. *Distribution of the patients among the different ages at which the disease appeared*



4 and 12 years than between 13 and 22. 15 patients in all became affected when over 30 years old.

In the literature, in studies of the age at which the disease sets in, the cases have usually been classified into five-year groups, beginning with the first year. It seems to me that this kind of classification does not always give a clear enough

picture of the distribution of ocular involvement among the various ages. Yet, to compare the results reported on the literature and my own, I drew up Table 1. on p. 30 with a five-year-group distribution.

TABLE 1

Age at which the patients developed interstitial keratitis, in the materials of some other investigators and my own material

Ages of the onset of the disease	Igersheimer	Herzau & Hossmann	Granström	Schweickhardt	Hoechne	Own material
1—5 yrs.	7,4 %	7,4 %	8,5 %	5,9 %	9,3 %	14,6 %
6—10 yrs.	26,6 »	21,2 »	30 »	28,3 »	31,5 »	35,9 »
11—15 yrs.	27,7 »	16,6 »	22,5 »	29,7 »	21,6 »	21,6 »
16—20 yrs.	17,5 »	25,4 »	19,5 »	21,9 »	17,9 »	15,7 »
21—25 yrs.	16,4 »	17,3 »	11,5 »	10,5 »	7,4 »	8,4 »

The Table shows a greater number of patients developing the disease between 1 and 10 years in my material than in those of other investigators, but a clearly smaller number, with the exception of H o e c h n e's figures, of patients who became affected with the disease between 16 and 25. It is difficult to explain the reason for this. Local variations or such as are due to time, the virulence of the spirochete and the patients' resistance, may occur.

4. Sex of the Patients

In the literature the disease has as a rule been found to occur much more commonly in female patients with congenital syphilis, which accounts for certain attempts to explain the pathogenesis of the disease (G a n g e and A n t o i n e). I g e r s h e i m e r, however, did not suppose that there were any noteworthy differences in incidence between the two sexes.

As to the distribution of the patients according to sex in the material from the Ophthalmic Clinic of Helsinki University, I noted that out of 451 patients 252, or 56 %, were female and 199, or 44 %, male. The difference is not very convincing. Several investigators (Cunningham, Holmes Spicer, Herzau & Hossmann and Klauder & Vandoren) mention that 60 % of the patients in their series were female. According to Härö there were in Finland 12 % more women among patients with congenital syphilis in 1943—1948 and as much as 40 % more than men among the patients who were over 20 years of age. Within the compass of my own material at least it would be presumptuous to claim, in the light of these figures, that interstitial keratitis is characterized by any larger incidence among female patients.

5. *On the Congenital-syphilitic Stigmas and Signs of Patients with Interstitial Keratitis*

In the diagnostics of congenital syphilis, so-called congenital-syphilitic stigmas and signs are of a special importance, which increases with the patients' age. According to Stokes, Beerman and Ingraham the diagnosis for congenital syphilis, after 20 years of age, must be made in more than half of the cases by purely clinical means. This is confirmed by my own cases also. The Wassermann, chol Wassermann or Kahn tests were positive for only 44 % out of my 109 patients whose mean age was 22.8 years at the time of the examination, and for 33 % of those among 109 patients who had been poorly or not at all treated.

Wile and Mundt noted one or several congenital-syphilitic signs in 86 % of the patients with late congenital syphilis admitted at hospital. Igersheimer found only 9 % of his 165 patients who were affected with interstitial keratitis free from other congenital-syphilitic stigmas and signs. In my own material I noted that only 9.4 % of 126 patients with interstitial keratitis were otherwise free from

these signs several (on an average 8) years after the keratitis.

Hutchinson's teeth, among which I included typical changes except on the cutting edge as well as the whole shape of the teeth, occurred in 57.5 % of my cases, which corresponds to the highest figures I have met in the literature (C a r v i l l and D e r b y 76 %, H o l m e s S p i c e r 44 %). *Mulberry molars* were noted in 10.2 %, which figure I find rather high considering that in a great number of my patients this dental change may have had an occasion to disappear. Thus mulberry molars occurred in patients whose mean age was at the moment of examination 14.7 years, about 3 times more frequently than among patients who were 28.5 years on an average when examined. I have not found in the works of other investigators any figures for comparison of the frequency of this symptom in patients with interstitial keratitis. The *saddle nose*, as a rule considered an important diagnostic sign, occurred in 8.7 % of the cases in my material, which is roughly in agreement with the figures I have met in the literature (H e r z a u and H o s s m a n n 8 %, S c h w e i c k h a r d t 10.9 % etc.). The saddle nose thus is relatively rare in my material and is surpassed in frequency even by such a slightly-known sign as the mulberry molar.

Rhagadic scars are sometimes a group of stigmas and signs which it is difficult to estimate. The principles of evaluation adopted by different investigators may often show variation even because of subjective factors. In my own material I took into account clear scar formations around the eyes and the nose and in the corner of the mouth and made a point of leaving out the cases in which it has been possible to interpret the scar formation in different ways. Proceeding like this I obtained a surprisingly high value, 40.2 %. I did not note any appreciable difference in frequency between young and older patients. The figures recorded by other investigators are markedly lower (C a r v i l l & D e r b y 11.7 %, S c h w e i c k h a r d t 12.3 %, H o e h n e 9 %, and S t o k e s 6.5 % for patients with late congenital syphilis without keratitis). Evident *poor bearing* which I have considered due to congenital syphilis,

occurred in 4.7 % of the cases, which figure I find unexpectedly low. Saul's percentage was as high as 35, Carvill and Derby's 19.2. Values corresponding to mine were obtained by for example Holmes Spicer (4 %) and Herzau & Hossmann (5.2 %).

The so-called *Clutton's joint sign*, considered by several investigators to be closely but thus far unaccountably associated with interstitial keratitis, was present in 10.2 % of the cases in my material. The total number of cases with joint symptoms was 16, in 15 out of which the symptom in question occurred before keratitis or during it and only once after, in this case after about 1 year. The figures recorded in the literature for this sign approximate mine and each other: Carvill & Derby 12.3 %, Igersheimer 20 %, Schweickhardt 7.3 %, Klauder & Vandoren 6.4 %. Klauder & Robertson noted the sign in 18 % out of 250 patients with interstitial keratitis and in 15 % out of 60 patients with congenital syphilis without any eye symptoms.

I examined the *sequel of periostitis* by palpation and inspection and in suspect cases by X-ray as well. The incidence thus obtained was 3.9 %. One patient exhibited it in both ulna and tibia, the rest in tibia only. Very variable figures are encountered in the literature: Carvill & Derby 35.1 %, Schweickhardt 6.4 %, Dalsgaard-Nielsen 8 %, Hoehne 11.1 %, Klauder & Vandoren 16.5 %. The value obtained by Stokes for patients with late congenital syphilis was 3 %.

The *forehead*, perhaps, shows changes typical of congenital syphilis more often than any other part of the face. So-called *frontal bosses*, the estimation of which, easily affected by subjective factors, is apt to vary, were a common sign among my patients, the percentage obtained being 19.7. Schweickhardt's percentage was 7.3, Hoehne's 8, Klauder and Wandoren's 6.4. The figure recorded by Stokes for his material was as high as 44 %. Among my younger patients this symptom was about 4 times more common than among the older ones, which would imply that some of the bosses disappear, partly at

least, with age. A high forehead extending sharply upwards and protruding forwards has also been considered characteristic of congenital syphilis. I met a forehead of this shape in 10.2 % of the cases. Carvill and Derby's figure was 13 %. — The forehead may also show another change which I have called the hair margin sign. In congenital syphilis the hair itself is often dry and brittle. Enroth described 3 cases with a diffuse hair margin and lanugo hairs on the forehead and cheeks. I have not found any detailed description in the literature of the way in which the hair margin in congenital syphilis may differ from the customary one. Yet I found that my own cases in this group conform to a certain rule. The horizontal hair margin as early as above the eyebrows ran directly downwards at the sharp angle which usually occurs on the temple (Fig. 3).

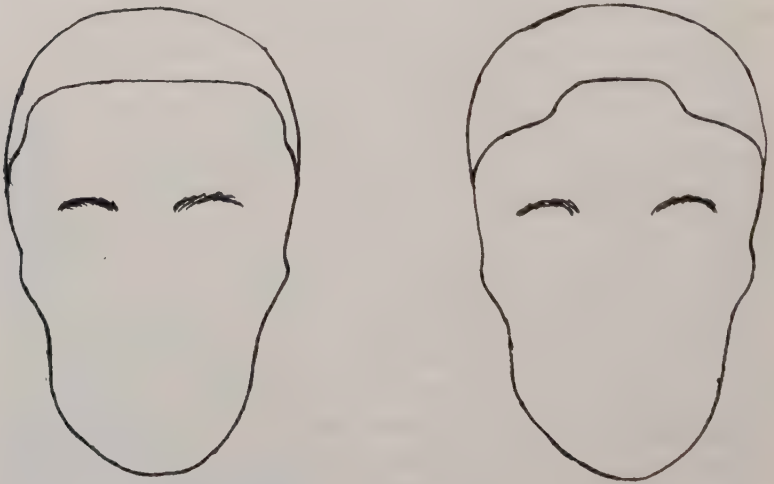


Fig. 3. *So-called congenital-syphilitic hair margin sign.*

Normal hair margin

Congenital-syphilitic hair margin

This change, I would say, does not belong to so-called syphilitic stigmas but is one of the same developmental anomalies as for instance the frontal bosses. When looking for a similar change elsewhere than in patients with congenital syphilis for several years, I found it in only one patient, a 10-year-

old girl, severely scrofulous, subjected to disturbances like those in syphilis, although they were caused by tubercle bacilli. I noted the hair margin sign in 8 patients out of 94, or 8.5 %, which proves that this symptom is a diagnostic criterion not unworthy of notice.

A symptom which has been given rather little notice is obvious *facial asymmetry*, a quite common sign. I noted in 6.3 % of the cases in my material. The asymmetry, clearly apparent in the denture also, is due to the non-analogous position of the facial bones as well as to their different size in the two halves of the face. The asymmetry may pertain to one single bone only, usually the mandible, but also to several facial bones at the same time. It may occur in all spatial directions. Most commonly one notes divergence from the normal in the course of the mandible towards the point of the chin.

The so-called *congenital-syphilitic facies* is often distinguished as a separate sign. This complex of symptoms, not easily definable, and due to many complementary factors, I noted quite clearly in 25.9 % of my patients. There are relatively few records in the literature on the frequency of the sign. Experienced investigators believe that they can identify congenital syphilis from this symptom in 90 % of cases. — Thickening of the medial part of the clavícula occurred in 4 of my patients, or 3.1 %. One patient had a cleft palate. I did not note ulnar deviation of the middle fingers, also held to be characteristic to some extent of congenital syphilis.

The observations described above of the frequency of different congenital-syphilitic stigmas and signs show their great diagnostic significance. Usually the same patient exhibits 2 or more signs. Only 21 out of 126 had only one of the signs mentioned. My material contained 5 patients with only one sign which sometimes could be accounted for in different ways, such as a congenital-syphilitic facies and rhagadic scars. I could not establish any connection between the age when the patient developed the disease, and the congenital-syphilitic signs, nor between the signs and vision. Only one patient, with severe obesity, had clear

endocrine disturbances. None of my patients showed any anomalies of the shape or functional disturbances of the thyroid. The female patients had no menstrual disorders.

6. *Changes in the Blood and the Liquor*

In cases of congenital syphilis serological tests are important in a much more restricted sense, both therapeutically and at a later age also for diagnosis, than in acquired syphilis. One Wassermann, cholWassermann and Kahn test on blood was undertaken in each of my cases, and likewise one Wassermann and cholWassermann on the liquor in 0.1 and 0.2 cc. My patients usually came for follow-up examinations from far-off localities so that control tests were ruled out for practical reasons. Since most of them were out-patients, liquor tests were done for only a small number, 40 patients in all.

In the follow-ups the Wassermann, cholWassermann or Kahn reactions were positive on the blood of 48 patients out of 109, or 44 % of the cases. The mean age of these patients, when examined, was 23 years. Out of 82 patients who had been given vigorous specific treatment the reactions or one of them were positive in 48 %, and only for 9 of the 27 patients who had been inadequately treated or not at all. Positive reactions were recorded for my patients to the following extent: WaR +, cholWaR +, Kahn + in 13 cases, or 27.1 %, WaR —, cholWaR +, Kahn + in 10 cases, or 20.8 % and WaR —, cholWaR —, Kahn + in 25 cases, or 52.1 %. In more than a half of the cases that were serologically positive only the Kahn was positive. Of the 25 patients in the last group 21 had received vigorous anti-syphilitic treatment.

No *examinations of the liquor* of the patients with interstitial keratitis had to my knowledge been carried out in connection with the follow-ups made. Yet an examination of this kind is very important prognostically and thus also from the social point of view. The significance of the liquor

tests has not been pointed out sufficiently in older ophthalmological literature, and only in the last ten years has there been any change in this respect. As far as I understand, it is just in older cases of congenital syphilis that an examination of the liquor is especially important. In my own cases, by force of circumstances, I had to content myself with only a small number of different liquor examinations: tests for the number and quality of the cells, Nonne and Pandy, Wassermann and cholWassermann tests. The 40 patients examined, however, give some kind of picture of the conditions in which neuro-syphilis occurs in patients with late congenital syphilis.

In the literature I have found fairly large percentages, mainly, to illustrate the incidence of neuro-syphilis in cases of congenital syphilis. Stokes, for example, noted an abnormal liquor in 20 % and clinical neuro-syphilis in 26 % of his cases, 33 % of his patients being over 14 years. White and Veeder's corresponding figures were 30.6 % and 17.8 %. The figures obtained by several other investigators are roughly similar. The liquor, as I said, was examined for 40 of my patients, of whom 2 exhibited pathological changes and both of them a positive cholWassermann. 8 of these 40 patients had not received any or only one combined series at the most of specific treatment, and no pathological changes were noted in the liquor of any of them. The frequency I noted was markedly lower than the ones usually mentioned in the literature. Only one of my patients had clinical neuro-syphilis.

7. Syphilis in Families

There were 7 illegitimate children among my 128 patients. I was successful in obtaining more detailed information of the family relations of 117 patients born in marriage. Naturally in such delicate matters as these it is not easy to get reliable information, and one should not draw inferences too readily and not very far-reaching ones from the results

obtained. On the other hand, the investigation I undertook showed that the patients or in case they were children the father and mother accompanying them, showed great understanding in the face of the often delicate questions I had to put, and the patients, besides, proved to be surprisingly well cognizant with what had taken place in the family, even of such matters as abortions. Though I am well aware of the many deficiencies of the results of my investigations which are based on past history, yet, because of the importance of the matter and a recognition of the value of some of the data obtained from the patients, I have presumed to present my results.

The average number of pregnancies that had occurred in the 117 families I studied was 3.9 to each family. Since the mean age of my patients was over 22 years at the time of the examination, the value may be taken as approximately normal. Accordingly, *pregnancies are almost equally frequent in the marriages of syphilitic parents as in those of healthy parents.* My figure corresponds to several values encountered in the literature: Hochsinger 4.2 to each family, Boas & Rönne 4, Sidler-Huguenin 2.9, Smith 5.2, and White & Veeder 3.9 to each family.

There were 8 *abortions* in my material, or in 1.7 % of the pregnancies. The percentage of White & Veeder for this was 15.2, those of Smith and Schweickhardt 13.9 and 3.5 respectively. My figure is probably too low but, considering the opinion I formed of the reliability of the information, yet surprisingly low. *Infant mortality*, calculated in relation to the children born alive, was also unexpectedly low, 23 cases out of 444, or 5.2 %. The values I found in the literature are as a rule considerably higher, e.g. Sidler-Huguenin's 20.2 %, White & Veeder's 20.4, and Schweickhardt's 36.1 %. Yet the corresponding value obtained by Härö for cases of congenital syphilis occurring in 1936—1947 is 3.3 %.

I took especial pains to find out to what extent the parents and brothers and sisters of my patients had been examined for syphilis. In 117 families either one or both parents had been examined in 29 cases only, in 19 of them both, in 9

only the mother and in 1 the father. The sero-reaction was positive before antisypilitic treatment for 92.9 % of the mothers and only 45 % of the fathers. My material, it is true, is rather small, consisting of only 28 examined mothers and 20 examined fathers, but the series I have found in the literature, in most cases, are approximately of the same size. White and Veeder, when examining mothers (182 cases), obtained 86.8 as the corresponding percentage. This percentage was 72 for Carvill and Derby's series comprising 55 mothers, and for Dennie and Pakula's 19 mothers 73.7. The figures recorded by these authors for fathers were: White & Veeder (38 fathers) 63.2 %, Carvill & Derby (30 fathers) 43 %, and Dennie & Pakula (10 fathers) 70 %. Of the patients' brothers and sisters 237 were alive at the time of the examination, 24.5 % of whom only had been examined to ascertain syphilis. Out of 57 living brothers and sisters examined 11 were serologically positive, or 19.3 % 194 younger brothers and sisters were alive and of these, all of whom might with great probability have contracted syphilis from their mothers, only 36 had been examined, as many as 30 being seronegative. 30 elder brothers and sisters of my patients had been examined and 22 of them reacted negatively. Out of my 106 patients 49 were first children of their families, 18 of them only children. 81 were first or second children. Thus the mean age of the brothers and sisters examined was somewhat lower at the moment of examination than the average age at which my patients developed the disease, taking into account that the time when the brothers and sisters were examined coincided with the onset of the disease in my patients. In this light the figures which illustrate the sero-negativity of the other children in the family appear unexpectedly high, and imply that only every 5th child in the marriages of syphilitic parents exhibited a serologically diagnosable congenital syphilis. According to the results I obtained *only 1/4 of the family members of patients with interstitial keratitis in this country had been examined for syphilis*, which shows that both socially and medically a great deal still remains to be

done in this important matter. I have not been able to find any figures in the literature for comparison in this respect.

Of the patients I examined 32 were married, and 18 of them had 40 children altogether, of whom again only 8 had been examined with a view to congenital syphilis. In none of the children of my examined patients, however, could syphilis be established either serologically or clinically. Only one of these 40 children was illegitimate. Among the male patients who were over 20 years, 8 out of 23 were married, and 15 of the 64 female patients.

Interstitial keratitis was very rare among the brothers and sisters of my patients. It occurred in 2 families only, in 3 brothers and sisters altogether, which is significant and contributes in bearing out the theory that congenital syphilis alone cannot explain the aetiology of interstitial keratitis.

Tuberculosis, supposed by some authors to have some significance, when coinciding with congenital syphilis, in the genesis of interstitial keratitis, did not occur more frequently in the patients of my material and their near relations than it does in this country on an average. 2 of the sisters of my patients and 12 of their parents had died of tuberculosis. — 2 of the patients had been treated at lunatic asylums, 1 of their sisters, 3 mothers and 1 father, all because of a mental disease due to syphilis.

8. *Occupation of my Patients and their Parents*

One often hears the view expressed that individuals affected with congenital syphilis are deficient to such an extent, both mentally and physically, that they mainly depend on the community for their living. Since my material afforded some possibility for going into this problem as well, I collected information about the occupations practised by my patients and their parents. Within certain limits, the occupation one has chosen may be considered a kind of criterion to one's intellectual standard. It is important to be aware of the background from which the patients

have started in life and what their social and economical qualifications have been for entering some special occupation. Evidently the majority of these patients had been handicapped not only by unfortunate social circumstances but also through inherited factors that were encumbering beyond the normal. I entered in the following Table the occupations of my patients and their parents side by side (Table 2 p. 41). Of the patients I inserted only those who had more or less made up their minds as to what career to follow.

TABLE 2

Distribution of parents and my patients among different groups of occupations

Occupation	Parents (135)	Patients (73)
Industrial workers and others of similar occupation	13,1 %	16,4 %
Unskilled labourers, including farm hands	47,6 %	34,2 %
Workers in business	1,1 %	13,7 %
Office employees and minor officials	7,9 %	9,6 %
Small farmers and farmers	20,9 %	10,9 %
Artisans (shoemakers, tailors, dressmakers etc.) ..	2,1 %	5,5 %
Persons with a university degree	0 %	4,1 %

According to the Table, unskilled labourers predominated clearly among the parents, while there were more individuals who had learned some trade, becoming either factory hands, workers in business and artisans, among my patients themselves. Office employees, officials and persons with a university degree are also more numerous among the patients. Only in the group of smallholders and farmers is the number of so-called skilled workers larger. As to the last group it should be noted that most of the persons entered in it are smallholders who get from agriculture only part of their living, which they eke out by various kinds of odd jobs. The number of illegitimates, as we

saw, was only 7. From my figures it is evident that *my patients have, on the whole, acquired a higher social status, i.e. a better occupation entitling them to one, than their parents have had.* This has been the case in spite of the fact that the parents have passed on to them hereditary qualities below the average, in spite of congenital syphilis and the restrictions imposed on their chances of development by poor social circumstances. Yet it should be remembered that the trend of development has with every year been towards greater specialization in every respect and towards prosperity. In any case my material shows that *patients with interstitial keratitis associated with congenital syphilis are in the main fairly good workers and acceptable members of the society.*

IV. Observations Made of the Eyes in Follow-up Examinations

1. *The Vision of my Patients in Follow-ups*

Whether vigorous antisyphilitic treatment administered in the active phase of the disease may have a beneficial effect on ultimate vision is a question which still remains open. Clausen even noted deterioration in 4 of the 23 cases he treated, in the course of the salvarsan therapy. Langendorff found that in his material (165 cases) the disease was always milder in the other eye if the patient had been given adequate antisyphilitic treatment before the other eye became affected. White and Veeder, when estimating the results of treatment for congenital syphilis, noted that even patients who had received appropriate antisyphilitic treatment developed interstitial keratitis. They viewed with pessimism the possibilities of treating late congenital syphilis with good results and wrote: »It is perfectly clear, however, that the treatment of late hereditary syphilis is far more disappointing than is that of infantile syphilis, and that in this condition time will effect many recoveries, both clinical and serological. The only satisfactory solution of the problem of hereditary syphilis is its prevention rather than its cure».

Carvill and Derby, when comparing the ultimate vision of patients treated antisyphilitically and those that were given no treatment, noted obviously better results in the group of treated patients. They declared that antisyphilitic treatment is clearly effective in preventing the other eye from developing the disease and in ameliorating its course in the other. They contended, on the other hand, that it

is very difficult, even impossible, to prevent the disease from breaking out, by antisyphilitic treatment. Holmes Spicer wrote that the results of antisyphilitic treatment were on the whole disappointing, and that it was incapable of arresting the course of the disease. Igersheimer examined 152 eyes several years after the active phase and took a suspicious view of the good results obtained by many investigators by specific treatment, although he could not deny its obvious effects in some cases. He considered salvarsan treatment a step forward, though not a radical one, compared with treatment with mercury. Weve, again, emphasized the importance of early and vigorous antisyphilitic treatment. Herza u and Hossmann argued that combined arsenic and bismuth treatment had effected no progress in view of results. Frazer, again, found that salvarsan had improved the results of the treatment of the disease. Seefelder agreed with the view that antisyphilitic treatment did not affect the course of the disease.

Cole, Usilton and Moore et collab. were among those who regarded antisyphilitic treatment as beneficial in congenital syphilis. Their material showed that this treatment, even when incomplete, was effective in preventing the outbreak of interstitial keratitis. The percentage of patients developing the disease fell in treated cases to 9 against 36 for the untreated ones. But with heavy metal alone without any arsenic the treatment proved ineffective as a preventative. Specific treatment given in time also precluded the other eye from becoming affected, and ultimate vision was much better in the group of those treated antisyphilitically than among those who were given no treatment. Schweickhardt examined the vision of 74 patients (148 eyes) at least 2 years from the termination of the active phase, and found that poor vision was primarily due to opacity of the cornea and refractive changes. Dalsgaard-Nielsen estimated the vision in 303 eyes in the course of his examinations. He did not find that antisyphilitic treatment had any manifest effect on later vision, on complications of the disease or disability caused by it.

Yet the author did not want to deny the value of specific treatment, especially in shortening the duration of the disease, although its effect did not always appear as clearly as some authors had declared. H o e h n e carried out follow-ups on 110 patients (194 eyes) and took a rather doubtful view of the effectiveness of both specific and nonspecific (fever) therapy. K l a u d e r and V a n d o r e n published an extensive investigation on the effect of different methods of treatment upon ultimate vision. In view of the great number of refractive changes noted after the disease the reliability of the authors' results is impaired by the fact that in a good many cases the vision was determined without correcting the refraction. These authors emphasized the propitious effect of specific treatment on ultimate vision, especially when administered in the active phase of the disease. The best results were obtained by combined arsenic, bismuth and fever treatment. The authors pointed out, however, that in view of the on the whole disappointing results from the treatment, prevention of the disease would be the best method.

K l a u d e r considered penicillin a step forward in the therapy of the disease, compared with arsenic. F o r s y t h considered penicillin equally effective in the treatment of the acute phase as combined arsenic and bismuth therapy. He found antisyphilitic treatment beneficial when given at the onset of the disease at once when the cornea showed initial oedema. F o r s y t h undertook follow-ups of 66 eyes, yet without correcting the refraction, and the observation time was relatively short, 4—23 months. G r a h a m, R o m a i n e and R u l i s o n believed that appropriate antisyphilitic treatment before the outbreak of the disease would alleviate its course and that ultimate vision would be markedly better in cases treated specifically than in those that were not treated. L o n d o n and N o o j i n treated 9 patients exhibiting interstitial keratitis with penicillin and fever therapy. They did not find that penicillin had any clear remedial effect. The subjective symptoms, however, disappeared soon. I n g r a h a m stated as his view that in the treatment of the disease penicillin was very nearly

as effective as combined arsenic and bismuth therapy. Not even penicillin was able to prevent the outbreak of the disease, nor the other eye from being involved nor a recurrence later.

In my own material I examined the vision of 126 patients (224 eyes). On the basis of vision, following on the whole Igersheimer's and Schweickhardt's system, I made the following classification: Excellent vision (visus = 1.67, 1.25 or 1.0), good vision (0.67 or 0.5), fair vision (0.33 or 0.25), poor vision (0.17, 0.13 or 0.1), counting fingers and blind (visus $\leq$ 0.01). Taking into account all eyes I drew up the following Table 3 (p. 46). For a clearer picture of my patients' actual vision I composed a similar Table entering only the vision of the better eye, with the result shown in Table 4 (p. 46).

TABLE 3

Vision determined in follow-up examinations, taking into account all eyes

	Excellent vision	Good vision	Fair vision	Poor vision	Counting fingers	Blind
Number of eyes	49	77	56	17	14	11
Percentage	21,9	34,4	25	7,6	6,3	4,9

TABLE 4

Vision determined in follow-up examinations, taking into account only the better eye

	Excellent vision	Good vision	Fair vision	Poor vision	Counting fingers	Blind
Number of eyes	38	47	28	7	3	1
Percentage	30,6	37,9	22,6	5,6	2,4	0,8

To elucidate the effect of antisyphilitic treatment on ultimate vision in my own material I divided my patients

into two groups: (1) those treated, who had been given combined arsenic and mercury treatment or arsenic and bismuth treatment in two successive series of 10 pairs of injections at least during the active phase of the disease and immediately after it, and (2) those treated less well or not at all, who had received at the most one series of the treatment mentioned. Out of the 87 treated patients 70 had been given 3 or more series of the treatment in question. Of the 32 patients in the second group 8 had received no antisyphilitic treatment and 15 only 2—5 pairs of injections. In the group of treated patients only 4 had been given combined arsenic and mercury treatment, the rest combined arsenic and bismuth treatment. The number of the patients treated with penicillin is thus far so small and the time over which they had been observed so short that I have omitted the cases from my material. From these findings, taking into account the vision of all eyes, I drew up Table 5 (p. 47). By recording only the vision of the better eye and dividing the patients into two groups I obtained Table 6 (p. 48).

TABLE 5

Vision in follow-ups, taking account all eyes, of patients given specific vigorous and slight treatment or none

	Treated 157 eyes	Slightly treated or not treated 59 eyes
Excellent vision	35 eyes = 22,3 %	14 eyes = 23,7 %
Good vision	50 eyes = 31,8 %	23 eyes = 38,9 %
Fair vision	43 eyes = 27,3 %	10 eyes = 16,9 %
Poor vision	10 eyes = 6,4 %	6 eyes = 10,2 %
Counting fingers	12 eyes = 7,6 %	2 eyes = 3,4 %
Blind	7 eyes = 4,5 %	4 eyes = 6,8 %

TABLE 6

Vision in follow-ups, taking into account only the better eye of patients given specific vigorous and slight treatment or none

	Treated 87 eyes	Slightly treated or not treated 32 eyes
Excellent vision	28 eyes = 32,2 %	11 eyes (34,4 %)
Good vision	31 eyes = 35,6 %	12 eyes (37,5 %)
Fair vision	23 eyes = 26,4 %	4 eyes (12,5 %)
Poor vision	1 eyes = 1,2 %	4 eyes (12,5 %)
Counting fingers	3 eyes = 3,4 %	—
Blind	—	1 eye (3,1 %)

The Tables show that *vision, when estimated for all eyes, remained excellent all through the disease in about 1/4—1/5 of the cases, and taking into account only the better eye in about 1/3. The good results obtained in inadequately treated cases and those not treated are especially noteworthy. 80—90 % retained a vision which could be deemed at least fair, and there was no appreciable difference between the treated patients and those who had received slight treatment or none. The small number of blind eyes, furthermore, is noteworthy. The vision recorded for my treated cases corresponds roughly with most of the results I have met in the literature. Yet Igersheimer's, Herzau and Hossman's statistics are less good. The patients of the former were mainly treated with arsenic and mercury, those of the two latter with arsenic and mercury or arsenic and bismuth.*

Several studies in the literature give figures on the later vision of patients with interstitial keratitis. On the other hand, I have encountered only 4 publications in which vision had been examined separately for patients who had been given specific appropriate treatment and those treated slightly or not at all. Since different investigators estimated the visual acuity from different distances and also classified the results differently, comparison of results presents some

TABLE 7

Follow-ups vision of patients given specific vigorous and slight treatment or none, in some investigators' and my own material

Treated	Eyes or cases	Vision % eyes	Vision % eyes	Vision % eyes
Carvill & Derby		1,0—0,28	0,2 —0,1	< 0,1
As + Hg	178 eyes	84,2	11,8	3,9
Dalsgaard-Nielsen		1,0—0,33	0,25—0,1	< 0,1
As + Hg, As + Bi	132 eyes	87	7	7
Klauder & Vandoren		1,0—0,29	0,29—0,1	< 0,1
As + Bi + fever therapy	63 eyes	68	23	10
Graham, Romaine & Rulison		1,0—0,29	0,25—0,2	< 0,1
As + Bi + penicillin	49 cases	78	12	10
Own material		1,0—0,25	0,17—0,1	< 0,1
As + Hg, As + Bi	157 eyes	82,2	6,4	11,4
Slightly treated or not treated				
Carvill & Derby	179 eyes	55,7	25,6	18,4
Dalsgaard-Nielsen	82 eyes	57	17	26
Klauder & Vandoren	185 eyes	51,1	37	12
Graham, Romaine & Rulison	—	30	23	47
Own material	59 eyes	79,7	10,2	10,1

difficulty. In my Table 7 (p. 49) I have tried to combine the results of the 4 studies just mentioned and my own so as to make them as accurately parallel as possible. For comparison I mention also Klauder's results, obtained with penicillin treatment, which are in rough agreement with those of Forsyth, achieved with penicillin and fever therapy: total number of eyes 97, vision 1.0—0.33 in 84.5 %, 0.25—0.1 in 11.3 % and < 0.1 in 4.8 %.

In a comparison of the results obtained by different investigators for *treated patients*, entered in Table 7, one

notes that they are very nearly similar. K l a u d e r and V a n d o r e n's figures are somewhat less good than those of the others. The results K l a u d e r obtained later, however, with fever and heavy metal and arsenic treatment are already on the level with the rest. It should be noted that K l a u d e r and F o r s y t h did not achieve any better results with penicillin treatment.

In the group of *inadequately treated or not treated patients* the values of different authors vary considerably. My own results, especially in the best vision group, are clearly in advance of the rest. The results reported by G r a h a m, R o m a i n e and R u l i s o n for inadequately treated patients, on the other hand, lag behind those of others.

Since ultimate vision is greatly affected by the lapse of time from the termination of the active phase of the disease, I took into account, like most investigators, only those cases in which this time was more than a year at least. The following Table (No. 8, p. 50) shows how many years elapsed in each case between the termination of the active phase and the moment when the patient was examined. On an average this time was 8.4 years. As regards the share of time in improving vision the patients are thus approximately on the same level.

TABLE 8

Time (in years) elapsing from the termination of the active phase of the disease to the follow-up examination

Time in years	1	2	3	4	5	6—10	11—15	16—20	21—25	over 25
Number of patients	20	4	11	5	7	39	15	14	18	1

Among my own groups of patients who were given specific vigorous and slight treatment or none the estimated vision was approximately similar. The differences were so small that no conclusions can be drawn from them in any direction. The unexpectedly good sight noted among slightly treated or untreated patients is not always, I find, very much

to be wondered. In spite of the considerable progress made in the treatment of syphilis in the present century, every antisyphilitic method of treatment, when tried, has had little effect on the course of interstitial keratitis in the acute phase. *Yet it is the nature of the acute phase that is most decisive in view of the patient's ultimate vision.* If no effect can be produced on it by antisyphilitic treatment, no appreciable results can be expected in view of the improvement of later vision.

2. Disability Caused by Interstitial Keratitis

To obtain a clearer picture of the reduction caused by interstitial keratitis on the patients' capacity for work, I estimated the degree of their disability in percentages on the basis of their vision. I calculated the disability percentage from Zeeman's Table, yet with the modification that when one eye was totally blind and the other had normal sight, I entered the percentage 20 instead of 15 in Zeeman's Table. This gave me the following Table, in which I separated, for comparison, the male and female patients into special groups. I also inserted in the Table the results of D a a l s g a a r d - N i e l s e n, the only accurate disability estimations for this disease that I have found in the literature (Table 9, p. 52).

The Table shows that *somewhat more than one half of my patients retained their full capacity for work as far as sight is concerned.* This is the more remarkable since I have put down as 0 % invalids even patients with vision 0.5 in both eyes. The number of slightly disabled patients is considerable, so that 0 % and 5 % invalids make up 70 % of the total number of patients. The remaining 30 % distribute themselves fairly evenly among the different disability groups, thus, however, that the number of 70—100 % invalids is smaller in proportion. No difference clear enough to justify

TABLE 9

Disability percentages estimated in follow-ups on the basis of vision, in Dalsgaard-Nielsen's and my own material

Dalsgaard-Nielsen's material

Disability percentage	Percentage of patients	Disability percentage	Percentage of patients
0	51	40	1
5	9	50	3
10	4	55	1
12	3	60	1
15	2	65	2
18	2	70	1
20	5	75	5
25	1	90	2
30	2	100	6

Own material

Disability percentage	Percentage of patients (125 pat.)	Percentage of 86 female pat.	Percentage of 39 male pat.
0	50	50,1	48,9
5	17,7	14,6	22,4
10	3,8	3,7	4,1
20	2,3	2,4	2,1
35	3,1	3,7	2,1
40	5,4	6,1	4,1
45	5,4	6,1	4,1
50	1,5	1,3	2,1
60	2,3	2,4	2,1
65	6,2	4,9	8,2
70	—	—	—
80	1,5	2,4	—
100	0,8	2,4	—

conclusions in one way or other is noticeable between male and female patients. The figures I obtained for my series are in approximate agreement with those of Dalsgaard-Nielsen. In his statistics, the more numerous occurrence of 70—100 % invalids attracts attention. To sum up, it might be said that *interstitial keratitis is a noteworthy factor conducing to disability among patients with congenital syphilis*, who so often are severely handicapped socially by this disease. *Yet interstitial keratitis seldom produces total blindness*. There were 11 blind eyes in my material, but only 1 blind patient.

3. Refractive Changes Due to Interstitial Keratitis

There has been a good deal of research on refractive changes following interstitial keratitis, though in most cases only some form of these changes has been studied. Carvill and Derby noted *myopia* in 29 %, Igersheimer in 28.9 %, Nordmann in 37.7 %, Saul in 53.3 %, Schweickhardt in 33.8 % and Dalsgaard-Nielsen in 32 % of their series of patients.

In my own material I examined 196 eyes, in which the refraction could be established. Myopia was revealed in 33 %, which corresponds to the values obtained by the authors just mentioned and *exceeds markedly the frequency of myopia (about 10—15 %) in healthy people*.

Hyperopia has seldom been met. Igersheimer noted it in 4.6 %, Nordmann in 9.4 % and Dalsgaard-Nielsen in 15 %. My own figure is 8.1 %, approximately in agreement. For healthy people the frequency of hyperopia is much higher, about 30—50 %.

Astigmatism has usually been established as the most common refractive change in this disease: Igersheimer 90.7 %, Saul 70.7 %, Schweickhardt 23 % and Dalsgaard-Nielsen 65 %. My own value is 37.1 %. For this I only took into account the cases in which a cylinder glass had really improved the vision. Myopic and

hyperopic astigmatism occurred in Dalsgaard-Nielsen's material in the ratio 25:15, while in my material the difference was much more obvious, namely 35 : 2. In the literature direct astigmatism is said to be somewhat more common than indirect. Igersheimer obtained for direct and indirect astigmatism the ratio 58.9 : 35.9 and Saul 56.6 : 43.4. My own figures show on this point as well a greater difference, 67:8. Oblique astigmatism occurred in Dalsgaard-Nielsen's series of patients in 41 % of all the astigmatic cases, and in my own patients in 24.7 %, which figure is lower than I expected in view of the quite irregular site of the corneal scars. A vertical or horizontal axis occurred thus in 75.3 % of my material and an oblique one in 24.7 %. These figures show that a change in the total shape of the cornea because of its cicatrization and that of surrounding tissue, especially the sclera and the iris, has a greater share in the development of refractive changes than local scar formations in the cornea.

Scar formation and atrophy following inflammatory changes in the anterior part of the sclera, which according to my observations are more common than has usually been supposed (see p. 72), *apparently contribute to development of astigmatism and myopia*, as does reduction, due to atrophy of the iris, of turgor in the inner parts of the eye. The refractive changes noted have as a rule been small, but because of opacities in the cornea less improvement of vision has been achieved with glasses than might perhaps have been expected. Nevertheless, in view of the disability, slight or considerable, due to reduction of vision which is a common consequence of the disease, correction of even a small refractive change has often been of great importance.

That the refractive changes caused by interstitial keratitis have often been so slight dioptrically, according to the few statements I have met in the literature (Schweickhardt and Dalsgaard-Nielsen) is partly due to the fact that the patients usually develop the disease at an age when the eye has on the whole reached its full development. In the following Table (No. 10, p. 55) I record my own observations of the degree of various refractive changes.

TABLE 10

Degree of different refractive changes in dioptries, noted in follow-ups

	Myopia	Hyperopia	Astigmatism
1—2 dioptries	38 eyes	13 eyes	62 eyes
3—4 dioptries	8 eyes	2 eyes	8 eyes
5—6 dioptries	6 eyes	1 eye	3 eyes
over 6 dioptries	11 eyes	—	—

My figures are in approximate accord with S c h w e i c k h a r d t's and D a l s g a a r d - N i e l s e n's values. Like D a l s g a a r d - N i e l s e n I found no connection worthy of note between sex and the incidence of different refractive anomalies. The number of the series of treatment given apparently did not affect the development of the refractive changes. To find out whether there was any connection between the age when the disease set in and the degree of the refractive changes, I studied the matter on myopic patients. In case of slight myopia there was no correlation. In stronger myopia (over 6 dioptries) on the other hand, there was an evident connection. *There were 11 eyes in all among my patients in which the myopia exceeded 6 dioptries, 6 of these eyes developed the disease at the lowest age noted for its onset in my material, 3 years.* In the other cases the ages of involvement were: 1 eye 7 years, 2 eyes 10 years; 1 eye 16 years, and 1 eye 22 years. Not much can be concluded from so few cases, but the age at the onset of the disease may be of some significance if it is a very early one, below 7, for the rest both slight and considerable refractive changes distribute themselves evenly among different ages of involvement.

4. *Recurrence of Interstitial Keratitis*

Not only the complete aetiology of interstitial keratitis but also the biological laws to which the disease conforms when recurring still remain unclear. Priester estimated with what probability each aetiological theory could solve the problem of recurrence. He found Schieck's theory the most plausible. According to Schieck a recurrence or recurrences were possible only if in the first inflammation the whole cornea had not been involved in the process. According to Priester, Igersheimer's theory took a great number of recurrences for granted, while Elschnig's and Löwenstein's did not allow, sufficiently, for the possibility of recurrence. Guy supposed that there was no essential difference between recurrences and actual interstitial keratitis. According to Holmes Spicer a slight local recurrence in the cornea might be due to the fact that all the spirochetes were not destroyed in the first phase.

v. Hippel mentioned 17.25 % as the incidence of recurrences. Holmes Spicer noted 9 % of recurrences in his large material. They were as a rule slight in nature, sometimes connected with some slight trauma, lactation or impairment of the general health. In one case Holmes Spicer noted a recurrence as late as 30 years after the first inflammation. Carvill and Derby found recurrences in 3.6 % of their 100 treated cases and in 27 % of those that had not been treated specifically. After three years' observation the corresponding figures were 3.6 and 13. The longest interval noted was 20 years.

Igersheimer set down recurrences only those cases where at least one year had passed without symptoms. The percentage of recurrences in his own material was 14. Usually the disease recurred 2—10 years after the first phase, but for one patient it took as much as 38 years. Whether appropriate antisyphilitic treatment was capable of preventing recurrence, Igersheimer could not say with any certainty. Out of 34 of his own patients with a recurrence only 5 had been treated against syphilis at some

time or other, all of them inadequately. Igersheimer, although he supposed that specific treatment made a recurrence less likely, noted recurrence also in patients who had become sero-negative. The recurrence was, however, slighter than the first phase, as a rule, and did not affect vision to nearly the same extent.

Prokopenko recorded recurrence in 4, or 8.3 % of his 48 patients, Granström in 5.5 %, Frazer in 9 % and Hoehne in 5.6 %. Herzau and Hossman's materials showed that compared with treatment with mercury and iodine combined arsenic and bismuth treatment did not reduce the number of recurrent cases of which there were 16 % in their material. Schweickhardt considered cases in which there had been a 2 years' symptomless interval at least, as recurrences. He found 7 such cases among 160. The recurrence was always slighter than the first phase. Cole, Usilton, Moore et collab. agreed with Carvill and Derby's view that antisyphilitic treatment was to some extent helpful in preventing recurrence of the disease. 14 % of their patients who had received specific vigorous treatment had recurrences and 29 % of those whose treatment had been specific but slight. In Dalsgaard-Nielsen's material there were 19 recurrences (5 %). The interval was 1—19 years from the first involvement. The author pointed out that not all congestions meant a renewal of the disease. Klauder and Vandoren noted 16 % of recurrences among 198 patients who had been given less than 20 pairs of injections of combined arsenic and bismuth treatment, while only 8 % recurred of 98 cases in which the patient had received over 20 pairs of injections of the same treatment. After the discovery of penicillin Klauder wrote that this drug was incapable of preventing recurrence, which was what Ingraham, too, had concluded.

Among my own patients (128 in number), I noted a recurrence in 16 cases, 12.5 %. In the three cases I was notified of the blood test, at the time of the recurrence, the Wassermann, cholWassermann and Kahn being positive in all the cases. These 3 patients had been given 5 and 6 and 5 series of com-

bined arsenic and bismuth treatment respectively during the active phase and immediately after it. The 16 patients mentioned had received series of combined treatment before the recurrence to the following extent: 3 patients had not received any, 5 patients 1 series, 2 patients 5, and 3 patients 6 series of treatment. For 3 patients no information was available on this point. Table 11 (p. 58) shows how soon after the termination of the active phase the recurrences took place in my cases.

TABLE 11

Appearance of recurrence after the termination of the active phase

Years from termination of active phase	1	2	3	4	7	9	11	13	15	16	17
Numbers of patients with recurrence	2	2	1	2	1	1	2	2	1	1	1

It is apparent from the figures that the lapse of time does not guarantee protection against possible recurrence of the disease.

In Table 12 (p. 58) we see the distribution of those of my patients who had a recurrence, among the different ages at which the disease set in, at the moment of the outbreak of the first phase of the disease.

TABLE 12

Age of onset in the first phase of the disease, of patients with recurrence

Age (in years) at which first phase began	3	4	5	6	7	8	9	12	13	16	18
Number of patients with recurrence	3	1	1	2	1	1	2	1	1	2	1

According to this table, the age at which the disease first appears is of no great importance in view of the recurrence later. It should be noted, however, that the number of recurrences was considerable in cases when the disease began at 3 years of age. There were only 4 patients who developed the disease at 3 years in the whole material.

There did not seem to be any appreciable connection between the amount of the antisyphilitic treatment given and the time at which the disease recurred. In my material there were recurrences in cases that had been treated specifically and appropriately, in slightly treated cases, and in those that had not been treated at all. In the treated cases the frequency of recurrence was 4.2 %, in the slightly treated or not treated ones 25 %. In spite of this difference, clear as it is, I would not presume to make any conclusive deductions as to the effectiveness of antisyphilitic treatment in preventing recurrence. Firstly, my material is quite too small, the periods of observation too short and there is a considerable number of recurrences among the cases in which vigorous antisyphilitic treatment had been given. The fact that not even 10 years' observation is enough is borne out by my Table, in which the recurrences are evenly distributed until the 17th year from the termination of the first phase.

5. About the Involvement of the Other Eye

Interstitial keratitis, as is well-known, is usually bilateral, but sometimes remains unilateral, often irrespective of whether the patient has been given appropriate antisyphilitic treatment or not. We do not yet know what laws govern the involvement of the other eye. Antisyphilitic treatment is incapable of preventing bilateral involvement. Most authors hold the view that the disease is slighter in nature in the eye that becomes involved later. Holmes Spicer considered it similar in both eyes. In 75 % of the cases the other eye was involved at the same time or within a year from the onset of the disease in the first eye. The interval was over 5 years in only 2 %. In patients who developed the disease at an early age the number of long intervals was greater. Holmes Spicer did not find there was any correlation between the severity of the disease and the length of the interval. Carvill and Derby noted that 82 % of their cases were bilateral and Carvill,

later, noted 74.6 % of bilateral cases in his series. Igersheimer considered that the other eye became as severely involved, though the disease usually lasted a shorter time. He could not say, from his own cases, whether this was due to the antisypilitic treatment. The other eye usually developed the disease either at the same time or within a few months. Gschwend found 70 % of his 116 cases bilateral and Nordmann, in the active phase, 47.6 % of 231 patients. In Dalsgaard-Nielsen's material (173 cases) 83 % were bilateral, and Hoehne's figure was 82.7. Among McLeod and Lemoine's 60 patients 40, or 68.3 % were bilateral.

In my material interstitial keratitis was bilateral in 81.3 % of 134 cases, of which 128 were follow-up patients, while information was obtained for 6 from the records of the Ophthalmic Clinic of Helsinki University. Since my patients were examined after the lapse of 8 years, approximately, from the active phase, bilaterality must actually have been still somewhat more common.

The right eye was diseased in 9 of the 25 unilateral cases and the left in 16. In 13 out of 134 cases the time between the involvement of the two eyes was half a year or more, in the rest less. The intervals were in these 13 cases: 1/2 year in 3 cases, 1 year in 2, 2 years in 3 cases, 5 years in 1, 6 years in 2, 11 years in 1 and 16 years in 1 case. Accordingly, the other eye would become involved within a year from the onset of the disease in the first eye in 92.7 % of the bilateral cases, which figure is considerably higher than Holmes Spicer's (75 %). If the involvements taking place within two years are taken into account, besides, the percentage becomes 95.4 of the bilateral cases. The interval was over 5 years in only 3.7 % of all the bilateral cases. This figure approaches the value recorded by Holmes Spicer. *On the basis of my figures one can predict as early as after a year, with considerably accuracy, whether the case is likely to remain unilateral.*

Of my 13 patients 3 were male and 10 female. In 5 cases the vision of the eye involved later had retained a better sight than the one first involved. In 3 cases the vision in

the eye where the disease had first appeared had remained better, and in 3 cases both eyes had preserved an equally good vision. In 2 cases it could not be established which of the eyes became involved first. *This small material of mine does not support the view that in the eye involved later the disease is nearly always slighter in character.* The patients in question had received series of combined treatment (arsenic + bismuth) in the interval between the involvements to the following extent: 4 patients had not been given any antisyphilitic treatment, 2 had received 1 series, 2 patients 2 series, 2 patients 3, 1 patient 4, 1 patient 7 and 1 12 series. For the patients who had not been given any antisyphilitic treatment between the involvement of the two eyes, the intervals were: for 1 patient 1 year, for 2 patients 2 years and for 1 patient 6 years. In these 4 cases at least, compared with the 9 cases treated specifically, omission of antisyphilitic treatment had not hastened the involvement of the other eye. In 2 cases out of these 4 the vision of the eye in which the disease appeared first was better, in one case the vision of the eye involved later and in one the visions of both eyes were equally good. *Among the 88 patients who had been given appropriate specific treatment 17 cases, or 19.3%, were unilateral and among the 32 treated only slightly or not at all 4, or 12.5%, unilateral, so that the differences are not convincing.*

6. *Is Antisyphilitic Treatment Capable of Preventing the Outbreak of Interstitial Keratitis?*

Just as there are greatly differing views about the significance of antisyphilitic treatment in interstitial keratitis, so there are also of its efficiency in preventing the outbreak of the disease. All authors admit that one can never be certain about the ultimate effectiveness of even vigorous antisyphilitic treatment in warding off the disease, but they disagree, especially, as to how much importance should be attached to the treatment in this respect.

Carvill and Derby declared that though anti-

syphilitic treatment was incapable of preventing the outbreak of interstitial keratitis, it did not lack effect when given in the course of the disease itself. v o m H o f e published 4 cases in which the patients developed interstitial keratitis in spite of the antisyphilitic treatment given previously. One of these patients responded negatively to the Wassermann test at the onset of the disease. C o l e, U s i l t o n, M o o r e et collab. studied this question on a large material. Out of 884 patients with late congenital syphilis 314 (36 %) came for treatment because of interstitial keratitis, and 90 % of them had had no treatment previously. Only 5 (2.1 %) of 243 patients who had earlier been treated specifically, i.e. with more than 15 injections of arsenic + heavy metal, developed interstitial keratitis. Even incomplete treatment, according to these authors, was to a considerable extent capable of preventing outbreak of the disease. The percentage of involvement was about 9 in these cases. Interstitial keratitis thus developed 3—4 times more often in cases treated incompletely than in those that were given full treatment. The authors supposed that treatment with heavy metal alone, without arsenic, was ineffective. Congenital syphilis had been ascertained in 98 patients out of D a l s - g a a r d - N i e l s e n's series, before the outbreak of interstitial keratitis, and not less than 17 reacted negatively to Wassermann after vigorous treatment. Penicillin, when it had been used for some time more widely against syphilis was found to be of as little effect as older drugs in preventing the outbreak of the disease (K l a u d e r, F o r s y t h, I n g r a h a m).

In my own material I had 8 patients who had been given antisyphilitic treatment before the outbreak of interstitial keratitis. 2 of them had received 6 series of combined antisyphilitic treatment prior to the keratitis. For one of the patients the Wassermann, the cholWassermann and the Kahn tests were negative at the onset of the disease. One patient, besides, had been given 2 combined series of treatment earlier. 3 patients developed keratitis after having been treated with at least one series. 2 patients manifested the disease about 5 years and 2 about 1 year after the termina-

tion of the antisyphilitic treatment. These few cases do not support the theory that antisyphilitic treatment is apt to provoke keratitis. None of my patients had received antisyphilitic treatment in infancy, and not until late congenital syphilis, when this treatment is generally considered to be relatively ineffective. These findings of mine, contributory to those some others described earlier, tend to confirm my opinion that *not much can be done by present antisyphilitic methods, at least not when they are used in late congenital syphilis, to counteract interstitial keratitis, its outbreak, course, or recurrence.*

7. *Interstitial Keratitis with Slight Symptoms*

E. Fuchs, in his text-book, wrote about cases of interstitial keratitis which ran a very mild course. Patches of quite slight opacity may appear in the cornea, and disappear again soon. There is no vascularization. Only little notice has been given in the literature to this kind of clinical picture. Holmes Spicer and E. Kraupa however, described a type of keratitis called abortive interstitial keratitis.

Because of the mild character of the disease most of the so-called abortive cases apparently do not present themselves in the ophthalmologists' consulting-rooms. But knowing how much the course of this disease may vary both subjectively and objectively there is no reason to doubt the existence of abortive forms. In my series of patients, brought together from out-patients' departments and hospital wards, there were no purely abortive cases. In 4 cases (8 corneas) the disease had run a very mild course and the corneas became quite clear.

Surprisingly often I noted that before coming for treatment for interstitial keratitis, my patients had sporadically exhibited slight congestion, sensitivity to light and dimming of vision, which disappeared without treatment within a few days. Such *predictive disorders*, so to say, might occur over a number of years before severer typical interstitial

keratitis. In a definite majority of my cases I could not refer the condition, with equal probability, either on the basis of data from past history or objectively, to any other eye disease. Possibly only a part of these patients developed interstitial keratitis of a severer type later, requiring treatment by a doctor or at a hospital. Perhaps in these instances the phase of the disease considered as a case of actual keratitis might have to be put down as a kind of recurrence in spite of being markedly severer in character than the first attack of the disease.

8. *Changes in the Shape of the Cornea*

A cornea which is *vertically elliptic* has been claimed to have some connection with interstitial keratitis and congenital syphilis. Igersheimer did not meet this form in any of his own cases. Saul, on the other hand, found a cornea of this type in as many as 13 of his 100 cases, and Hoehne in 7 out of 162. Hoehne pointed out that this change was present only in cases of simultaneous congenital syphilis and keratitis in the same patient and found that his 2 cases suggested that there might be some connection between this corneal change and ocular tension. Since not a single one of my patients had a vertically elliptic cornea, my material shows the anomaly to be much rarer than Saul's and Hoehne's findings would make one suppose.

No *keratoconus*, which sometimes occurs after interstitial keratitis, was met in my cases. Igersheimer believed that the keratoconus possibly present in the active phase usually subsided later. Hoehne saw this anomaly in one patient, Saul likewise.

Microcornea has also sometimes been connected, causally, with interstitial keratitis associated with congenital syphilis. Saul noted one case among his 100 patients. I have met with 5 microcorneas, in all of which the diameter was less than 9 mm, the smallest being 7.7 mm. One of my cases

was unilateral. In all of these cases both eyes became affected simultaneously. The ages of involvement were 5, 7 and 13 years. The vision was: 2 eyes = 1.0, 1 eye = 0.5, 1 eye = 0.25 and 1 eye = 0.01.

9. Changes in the Sensitivity of the Cornea

The cornea, as is known, is furnished with extremely sensitive tactile organs. In the absence of vascularization its nutritional balance is easily undermined and its capacity to form antibodies is slow. To counterbalance all this the cornea is supplied with a dense network of nerves, running in the anterior part of the parenchyma and in the epithelium. The corneal nerves branch out from n. ciliaris and enter from the direction of the limbus in about 60—70 branches into the corneal parenchyma where they lose their myelin sheaths. After a short run the nerve fibres perforate Bowman's membrane and form a so-called subepithelial plexus between it and the epithelium. From this plexus short fibres penetrate intercellularly into the epithelial layer thus giving rise to a so-called interepithelial plexus. The actual terminus of the nerve fibres is in the epithelial cells where they end with special terminal organs. Terminal organs are only met with in the epithelial layer. In the parenchyma one sees nerve fibres terminating without any actual terminal organ. Nearly every epithelial cell has a terminal organ of its own. Besides this nervous system there is another in the limbal parts of the cornea. From the pericorneal plexus of the conjunctiva and the sclera nerve fibres penetrate into the cornea for 1 $\frac{1}{2}$ mm, running under Bowman's membrane, and there they form a so-called superficial, paramarginal plexus which is connected with the network of nerves described first. This plexus, also, supplies the anterior part of the parenchyma with free neural ends and the epithelium with terminal organs. No nerves have been observed in the posterior part of the parenchyma.

Numerous papers have been brought out on the sen-

sitivity of the cornea in different diseases, but surprisingly enough there are none among them to describe any changes in sensitivity that might have been caused by interstitial keratitis. With a view to the great number of changes in the epithelium and the parenchyma that have been described in patho-anatomical investigations, one might well expect changes in sensitivity to follow the disease, especially reduction of sensitivity. Even the clinical picture of the disease seems suggestive of the peripheric origin of the infiltrations and their course from there towards the centrum, involvement of the whole cornea, and chronic character of the disease.

In my own material I examined the sensitivity of 71 corneas altogether, in all of which the opacities varied from thin maculae to dense leukomas. I used Frey's method for my tests, preparing different kinds of irritative hairs. I mounted a 2—4 cm long baby's hair and one of equal length from the horse's tail on a 10 cm long thin wooden splinter, to stick out parallelly with the splinter. I measured the capacity of pressure of each hair with $\frac{1}{2}$ mmg accuracy in micro-scales, and their diameter by micrometry and microscopically with 1/1000 mm accuracy. Out of the irritatory hairs prepared in this way I selected 3 different ones: 0.18 g/mm, 0.27 g/mm and 0.50 g/mm, and tried them on 20 normal healthy corneas. With the hairs 1 (0.18 g/mm) and 2 (0.27 g/mm) I obtained on each of the normal corneas a slight but unmistakable irritatory reaction, which was very marked with hair 3 (0.50 g/mm). Zitting (1932) tested the sensitiveness of the cornea on trachoma patients. According to her investigations, also, my hairs 1 and 2 would correspond to normal corneal sensitivity, while only hair 3 showed its clear reduction.

On 70 out of the 71 corneas examined I obtained a clear though slight reaction with hair 1 and for only one cornea was hair 3 the only one to produce a reaction. On the 70 corneas which had retained an approximately normal sensitivity no difference was noted in sensitivity between clear tracts and scars. The only cornea (Case Rec. 573/49) whose sensitivity was obviously reduced was dotted through-

out with opacities of medium density and the sclera was atrophied to such an extent that staphylomatous areas were numerous. Ocular tension was strongly reduced ($T = 5$ mm/Hg).

The results I have here described are in complete contrast to what I expected when starting my investigations. These findings possibly afford one explanation to the fact that the cornea of a patient with interstitial keratitis heals so well after a lengthy and often extremely severe inflammatory condition. They also perhaps account partly for the relatively good operative results obtained by corneal transplantation. Elschnig, Vannas, Franceschetti & Bischler, Löhlein and Roberts, report on success in 50 % of their cases.

It has been recognized for a long time that corneal metabolism and the nervous system are in close connection. Doggart declared that all corneal nerves may on the whole be considered trophic at the same time. *The fact that normal sensitiveness outlives interstitial keratitis is thus to some extent indicative of the relatively good preservation of the metabolism of the cornea and especially its epithelium.* My results also seem to imply that more damage is caused by the disease to the deeper layers of the cornea than the more superficial ones where the neural network has its site.

10. Other Changes of the Eye

When examining my patients with interstitial keratitis I observed other changes of the eye as well, whose causal connection with congenital syphilis and interstitial keratitis has not always been a matter of course in the same way. However, since in the literature they have often been considered as due to congenital syphilis, either directly or indirectly, I shall describe them here.

Strabismus concomitans was noted by Sidler-Huguenin in 14.4 % of his 125 patients with congenital syphilis, all of whom exhibited specific fundal changes.

Schweickhardt recorded 15 as the percentage for this anomaly in his patients with interstitial keratitis, and in over one half of the cases the strabismus was of the divergent type. Among my own patients 13, or 10.2 %, had strabismus. The corresponding incidence is said to be about 0.5—2 % among healthy people. 8 of my patients had received appropriate antisyphilitic treatment. Divergent strabismus was noted in 10. For healthy patients with strabismus 4 : 1 has been set down as the ratio of the incidence of convergent and divergent types. In 8 of my cases strabismus developed after keratitis, and in 6 of them it diverged.

Myopia or myopic astigmatism was noted in 7 of my patients with strabismus, 5 of whom squinted divergently. In 7 cases the vision of the squinting eye was below 0.1, and in one of them the bad vision was primarily due to changes in the eye fundus. From what has been said above, concomitant strabismus, which is usually divergent, seems to be indirectly attributable to interstitial keratitis. This strabismus may be caused by a shift in refraction towards myopia, on the one hand, and of impairment of vision due to corneal opacities and changes in the eye fundus on the other.

According to Igersheimer, *paralysis of extraocular muscles* is very rare in congenital syphilis. Paralysis of n. abducens occurs most commonly. McLeod and Lemoine considered paralysis of the extraocular muscles infrequent also. Out of my patients 3 had paralytic strabismus, or 2.3 %. In 2 cases it was a matter of paralysis of n. abducens and in 1 of n. trochlearis. In one of the cases where n. abducens was paralyzed the paralysis took place only after the active phase of interstitial keratitis was over.

Very variable *changes of the pupil* are met with in congenital syphilis. Especially in case of changes of shape and size it is often difficult, sometimes even impossible, to distinguish between what is pathological and what is physiological. Sidler-Huguenin noted disturbance in the reaction of the pupil in 12 % of his cases. White and Veeder found among their 246 patients with late congenital syphilis 6.1 % whose pupils differed in size bilaterally. Igershei-

mer regarded internal ophthalmoplegia as the commonest change in congenital syphilis. According to him absolute rigidity of the pupil was a fairly common change in this disease, while reflectory rigidity was so rare that he had encountered it in one patient only. Igersheimer found that pupillary changes were especially common in interstitial keratitis patients, although in the majority of the cases there was no actual connection between the two conditions. According to Herzau and Hossmann 0.5 % of patients with interstitial keratitis suffered from internal ophthalmoplegia. Saul noted absolute or reflectory rigidity of the pupil in 15 % of his cases. Hoehne found pupillary changes in 4.9 %.

My patients exhibited pupillary changes in 11 cases altogether, or 8.8 %. In 2 cases I noted absolute and in one case reflectory rigidity of the pupil, in the rest only change of its size and shape.

McLeod and Lemoine had noted *ptosis* in only one of the 60 patients with interstitial keratitis. Of my 126 patients 3 had ptosis, slight in each case. There were no other contemporary disturbances of the central nervous system. In one case the ptosis was bilateral. In all cases the ptosis had occurred before the outbreak of keratitis.

Sidler-Huguenin found *nystagmus* in 10.4 % of his patients and Saul in 1 %. Igersheimer believed that congenital syphilis could give rise to nystagmus in an otherwise symptomless eye, which quite likely was curable by antisyphilitic treatment in an early phase. Only one of my patients, or 0.8 %, had nystagmus. The condition had in this case persisted since birth, and this patient suffered from another disturbance of the central nervous system as well, paralysis of n. trochlearis, apparently also from birth. The vision of the eyes was: right eye = 0.33, left eye = 0.13. The poor sight was primarily due to corneal opacities.

Igersheimer attributed about 50 % of the *diseases of the lacrimal passages* occurring between 2 and 14 years of age to congenital syphilis. Acquired syphilis, on the other hand, seldom caused disorders in these organs. Purulent inflammation of the lacrimal sac occurred in 3 of my

cases. It was bilateral in 2. It first appeared when the patients were 6, 11 and 23 years respectively. None of them had been given appropriate antisymphilitic treatment before the involvement of the lacrimal passages. There were no pathological changes in the noses of any of the patients.

Langendorff noted, in follow-ups, increase of *ocular tension* in 6 out of 165 patients, or 3.6 %. According to Holmes Spicer there are very rarely any pathological changes in tension after the active phase. Igersheimer had often come upon temporary changes in the active phase of the disease, fall of tension in 21.7 % and increase in 27.4 %. The changes ranged within the limits 3 and 50 mmHg. Igersheimer, however, did not think these changes were due to the iritis noted in association with the disease. He believed hypertension to be very rare after the active phase. Herzau and Hossmann noted pathological increase of tension in the active phase in 21 out of 433 patients of whom 3 suffered from a disorder resembling buphthalmos. Schweickhardt agreed with Igersheimer in declaring that pathological increase and fall of ocular tension was fairly common in the active phase. Later, instead, he found hypertension in 3 cases only, out of 156. Dalsgaard-Nielsen considered that interstitial keratitis had caused increased tension afterwards in only 2 cases out of 173.

In my own cases I noted pathological increase of tension in 2 eyes (2 patients) and fall of tension in 3 (3 patients). In both cases with increase the eyes showed severe late changes. In one eye leukoma appeared in the centre of the cornea and there were numerous staphylomatous areas in the sclera. The other eye, again, was affected with extensive adherent leukoma of the cornea. The ocular tensions were 50 and 40 mmHg respectively and vision was = 0 in both eyes. In all the hypotonic eyes there was dense cicatrization in the cornea and an abundance of deep blood vessels. In 2 hypotonic eyes Descemet's membrane showed clear folds. Vision and tension were respectively: 0.08 and 5 mmHg, 0.06 and 8 mmHg, 0 and 5 mmHg. In the last-mentioned eye, where there were no folds in Descemet's

membrane, the pupillary membrane was dense, indicating that severe iritis had coincided with the active phase. Severe late changes and poor vision were common features of all these hyper- and hypotonic eyes. There was apparently no connection between the age of involvement and the changes in tension, but the severity of the disease no doubt was a significant factor. My few cases showed probable causality between hypotonia and folds in Descemet's membrane. It seemed probable that in all these cases the tensional changes were due to interstitial keratitis and especially to the accompanying iritis.

Congenital syphilis may also cause *night-blindness*, which then usually coincides with a clinical picture of the eye fundus simulating Sidler-Huguenin's fourth type, mainly characterized by changes of the pigmented epithelium of the retina. Quite considerable functional disturbances are sometimes met with in slight ophthalmoscopic findings. Sidler-Huguenin considered the lead-greyish colour of the central part of the eye fundus a very typical change.

I noted night-blindness in only one patient, who had had it as long as he could remember. Carle's adaptometer recorded his adaptation as considerably below normal. Day vision was normal in both eyes. There were slight changes in the eye fundi, in the periphery, in the form of small light patches and small particles of pigment. For all that was known there was no night-blindness in the patient's family so that in my case the condition may have been caused by congenital syphilis. Great functional disturbances occurred here in spite of the slightness of the ophthalmoscopic changes.

A fact noticed by v. Hippel, already, and one that strikes anyone studying interstitial keratitis, is the apparent complete lack, in many cases, of clinical symptoms in the *sclera* regardless of the comparatively numerous changes that are usually revealed in it in patho-anatomical investigations. Very little notice has been paid in the literature to the scleral symptoms accompanying interstitial keratitis. This may partly be due to the circumstance that even with a slit lamp it is difficult to obtain a view of and to estimate these changes. Patho-anatomical examinations have revealed

in the sclera infiltrations, especially around the blood vessels perforating it, and, besides, new vascularization. In contrast to Löwenstein's theory that obliterated vessels in the tissue surrounding the cornea give rise to nutritional disturbances and thus bring on interstitial keratitis, most investigators have not noted any obstruction of the pericorneal vessels of the sclera.

When looking for possible changes in the sclera I was struck by an interesting circumstance. The holes through which the vessels entered the sclera near the cornea appeared to me larger in some cases and the scleral tissue around them thinner than I have usually found it to be in normal cases. Admittedly, any estimation of a finding like this is difficult, but yet I would presume to contend that *atrophy*, as I prefer to call the phenomenon, *is as natural a consequence of the disease in the sclera as it is in the cornea, uvea and retina*. With only such vague criteria to judge from it is difficult to give any exact figures, but it seems to me that about 1/4 of my cases showed signs of atrophy of the kind described. In one eye (Case Rec. 207/49) I noticed another change in the sclera which I am inclined to put down as atrophy. About 3 mm from the limbus at 2 o'clock was a hole 2 mm in diameter with no vessel passing through it and through which the uveal tissue shimmered darkly. It was possibly a case of initial scleral staphyloma. In another eye (Case Rec. 573/49) I saw very severe scleral staphyloma with a number of protrusions, 3—4 mm in diameter. In this eye the ocular tension was increased and the sensitivity of the cornea clearly reduced. From different patho-anatomical studies and my own clinical findings I am inclined to believe that changes, especially atrophic ones, are more frequent in the sclera after interstitial keratitis than has been supposed till now.

V. Biomicroscopic Follow-up Examinations

1. *Changes in the Cornea*

a. Changes in the Epithelium and the Zone of Bowman's Membrane

The changes noted in the corneal epithelium and around Bowman's membrane after the active phase of interstitial keratitis vary greatly in character and have not been dealt with earlier within the compass of sufficiently large series of patients.

Considerable patho-anatomical changes are met in the epithelium both in the active phase and later, while Bowman's membrane remains almost intact. Disintegration of the epithelial layer (Seefelder, Bentele) is one of the characteristics of the conditions following the disease. The thickness of the epithelium varies markedly, the layer consists in places of only a few cells, and the form and size of the cells has changed. Leukocytes or lymphocytes occur between the cells, especially in the deeper layers. Rupturing (Elschnig, Jaeger, Igersheimer, Weskamp) is sometimes noted in Bowman's membrane and also creasing (Igersheimer).

One change, which occurs in the epithelium and below, associated in a way, as a part of the process, with corneal vascularization, is the shifting of the vascular arcades of the limbus towards the centrum of the cornea. I noticed this shift in only very severe cases, in which there was characteristic but strong vascularization of the parenchyma at the same time. In one case (Case Rec. 207/49) I was able to follow this shifting of the vascular arcades. It occurred

during retrogression and involved about $1\frac{1}{2}$ mm of the cornea. In the left cornea of the same patient I saw near the limbus, in the interpalpebral space, subepithelially, a girdle formed of small white points, resembling arcus lipoides. It was separated from the limbus by a clear corneal zone, about $1\frac{1}{2}$ cm broad (Fig. 4). The girdle resembled closely the so-called white limbus girdle described by Vogt, the pathogenesis of which still remains an open question. Berliner supposed that one possibly had to deal with a dystrophic change of hereditary origin. As far as I have noted no one has connected this girdle, earlier, with inflammatory diseases. I am inclined to believe that in my case interstitial keratitis was not wholly without a share in the genesis of the change in question.

Small point-like scars resembling so-called calcium patches in the anterior part of the parenchyma occurred subepithelially in one cornea (Case Rec. 738/48). They formed ring-like figures, 1—2 mm in diameter (Fig. 5). These changes, again, resembled Coats's white rings, whose genesis, like that of the change described above, has remained unexplained. Coats believed that these changes were hereditary. Vogt, on the other hand, thought that trauma had some share in their development. Ballantyne supposed that they were due to calcium degeneration. In my own cases the rings formed by white points occurred in the centre of the cornea and there was no dense scar

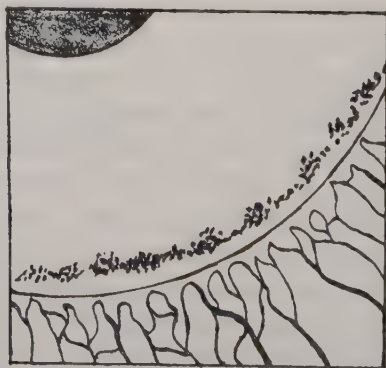


Fig. 4. *White limbus girdle of the cornea*

at the corresponding point in the parenchyma. Deep blood vessels had no connection with the rings. No noteworthy pathological changes were seen at the spot in the epithelium.

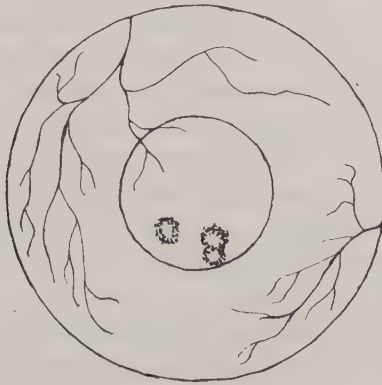


Fig. 5. *White rings of the cornea*

It has been known, for a long time, that a yellowish-green line may sometimes occur in the epithelium and below it in the zone of Bowman's membrane. Its appearance as a physiological senile corneal line was first described by Hudson in 1911 and by Stähli in 1918, after whom it has later been called the Stähli-Hudson line. Besides in connection with scars and as a physiological symptom this pigmented line has also been noted in keratoconus and in various inflammatory conditions of the cornea and the deeper parts of the eye. It has been believed that the line remains unchanged for years, even decades. The scar line, the senile line, and the ring line of Fleischer's keratoconus, according to many authors, follow a similar development, which like the chemical consistency of the line, still remains an unsolved question. Stähli supposed that the line developed from the alkali haematin of the lacrimal fluid. Grüninger noted a rupture of Bowman's membrane in the case which he examined patho-anatomically. Vogt attributed the senile line and the scar line to a rupture of Bowman's membrane caused by flattening of the cornea, and explained the appearance of the senile line as a phenomenon induced by hereditary factors. He

distinguished between 3 different types of pigmented lines of which the first, the most common one, was characterized by a bottle green colour with a tinge of olive yellow, diffuse edges and homogenous structure. M o n c r e i f f, likewise, thought that the actual cause of the appearance of the line was to be sought for in a rupture of Bowman's membrane.

In my own material I noted a pigmented line in 16 corneas, or 8.9 % of the cases, and in 3 of the corneas 2 lines simultaneously. The lines usually ran horizontally and were 1—3 mm long. My cases were of the so-called V o g t's first type, with the exception of one which differed from all types described so far. The patient was a 24-year-old farm hand (Case Rec. 207/49) who had developed bilateral interstitial keratitis about a year ago. 2 pigmented patches appeared in the cornea of his left eye, one of them resembling V o g t's first type, the other roundish and with diffuse borders. The possibility that the original line-like shape might have developed into a round one in the latter case is not quite compatible with the generally prevailing idea of its permanent character.

I did not find that there was any interrelation between the age when the disease set in and the appearance of the pigmented line. In all the cases when I noticed the line the disease had been severe and both corneal scars and deep vessels were more abundant than usual. *I am therefore disposed to think that in my cases the pigmented line in question is indicative of some kind of corneal degeneration, some inferiority of the tissue.*

In his new text-book on biomicroscopy B e r l i n e r puts down V o g t's white limbus girdle and C o a t s's white rings as belonging to so-called dystrophic changes of the cornea. The pigmented line, it seems, may also be accounted for as a kind of degenerative change. This interpretation is supported by S t ä h l i's and V o g t's theories of the analogous origin of different pigmented lines. *All the changes in the epithelium and in the tract of Bowman's membrane that I have described may thus apparently be regarded not as specific to interstitial keratitis, but as signs indicative of corneal degeneration.*

b. Changes in the Parenchyma

A great deal of research has been done on the permanent changes in the parenchyma which result from interstitial keratitis associated with congenital syphilis, but the investigators have based their observations on relatively few cases.

The corneal *scar* is the most manifest though by no means the most typical of these changes. It is the commonest cause for the poor sight that interstitial keratitis gives rise to. In the 178 eyes which I examined the bad vision of only 9 was due to some other cause (in 5 eyes to changes in the eye fundus and in 4 to atrophy of the optic nerve). Only after a relatively long lapse of time since the active phase can the cornea be expected to have cleared up into its ultimate condition, according to E. F ü c h s not until after $\frac{1}{2}$ —1 year.

Patho-anatomical changes are encountered in all layers of the corneal parenchyma. Some authors (Gilbert, Weskamp) find that the more superficial layers of the cornea suffer severest damage, others again (v. Hippel, Watanabe, Kunze, Igersheimer, Seefelder) that this happens to the deeper layers. The lamellary structure of the cornea is usually preserved well (Kunze, Seefelder et al.), but the interstices between the lamellae as a rule widen. Cells of most different kinds are met in the cornea: round cells, resembling lymphocytes, fixed corneal cells, epitheloid cells, less frequently eosinophil and giant cells. Blood vessels are usually noted in all layers and around them one often meets the strongest infiltration (Gilbert, Kunze, Seefelder et al.). Even necrotic patches are seen sporadically (Elschnig, Jaeger).

The scars in the corneal parenchyma may differ considerably in form, size and density. Their location also varies. In abortive cases they are hardly discernible afterwards. More superficial scars clear up more completely after the disease than those that are near Descemet's membrane. Vogt noted in keratitis and even afterwards sheet-like layers of opacity, one or even more. So-called calcification and dullish white fatty opacities are sometimes seen

in the scars, besides. Holmes Spicer describes a certain type of calcifying opacity in which a dense white and fairly large formation was seen in the surface layers of the parenchyma. There were clearer holes in its centre, and a zig-zag line. Holmes Spicer noted, besides, circles formed by scars, and a rare type of scar, a network formed by delicate subepithelial lines in the centre of the cornea, with small nodes at the crossings.

The classification of the scars according to their character, density first of all, presents some difficulty, for there is a great deal of variation on this point and estimation is affected by subjective factors. I do not find the old classification, nubecula, macula and leukoma a very happy one in old cases of interstitial keratitis. One notes some inconsistency in the literature on this point. Schweickhardt distinguished between 2 scar formations only, an ordinary macula and a dense leukoma. Dalsgaard-Nielsen classified the scars into the following groups: macula, denser macula and leukoma. For my own material I have used the following classification: diffuse or smoke-like macula, patch-like macula and leukoma. I did so after having found that a smoke-like macula, dissolving itself into the surroundings without any distinct border, often fairly large, seems to be quite typical of the disease. This smoke-like opacity, in contrast to the patchy macula and leukoma, which are usually met deeper down, occurs in all parenchymal layers and has its site mainly in the centre of the cornea.

Corneal scars are closely associated with corneal atrophy, which is disclosed by biomicroscopy and is characterized by unevenness of the corneal surface as well as the fact that the cornea becomes thinner. Dalsgaard-Nielsen noted atrophy in 15 % of his cases, in which the cornea had been reduced to $1/2$ — $2/3$ of its normal thickness. In my own material I did not separate the atrophic corneas into special groups, for I found an estimation of the atrophy from the thickness of the tissue only, unreliable, and secondly, because the thickness of the cornea nearly always varies wherever there is a denser scar, which makes an evaluation of the total atrophy difficult when the condition occurs in

many patches. To me it seems that atrophy can be estimated from the density and size of the scars as well as the thickness of the cornea. My findings of the different scar formations compared with the results of Schweickhardt and Dalsgaard-Nielsen are shown in the following Table (No. 13, p. 79).

TABLE 13

Frequency of occurrence of different corneal scars in the author's and Dalsgaard-Nielsen's and Schweickhardt's material

Type of scar	Author's material	Dalsgaard Nielsen's material	Schweickhardt's material
Patch-like macula	54,5 %	} 81 %	—
Smoke-like macula	37,1 %		—
Leukoma	3,9 %	5 %	2,7 %
Completely cleared cornea	4,5 %	14 %	—

I found somewhat more maculae than Dalsgaard-Nielsen, perhaps because in my material the cases were of a more severe type, and also because I took into account the smoke-like macula which sometimes may be very faint and therefore easily overlooked. Leukomas occurred with almost equal frequency, rather seldom, in all three materials, which is in agreement with the view held by most authors that interstitial keratitis rarely leads to very poor sight or blindness. I noted chalk white so-called calcium patches which sometimes occur in scars, in 5 eyes, or 3.9 %, and they distributed themselves evenly among the different ages of involvement. I did not note any interrelation between age of involvement and the other types of scar, either.

More typical than scars are the permanent *blood vessels* of the parenchyma, the site and course of which is a valuable criterion though not sufficiently made use of, in the diagnostics of the disease. Klauder and Cowan emphasized their importance and pointed out that the deep blood vessels

remaining in the cornea were sometimes, at a more advanced age, the only signs of congenital syphilis that were left.

Holmes Spicer gave in his monograph a detailed description of the deep blood vessels. He distinguished between different types of vascular ramification, calling them brush-like, tree-like and flower-like types. Sometimes he noted branching out of the deep vessels from a special large trunk. All these types could persist as such or as obliterated vessels, for years. Offret and Chauvet distinguished between 7 different forms of interstitial vascularization of the cornea, of which the brush-like and the filiform were especially characteristic of syphilitic keratitis. Kleefeld always saw in the cornea deep blood vessels in old cases of interstitial keratitis and therefore thought in questionable whether the disease could ever be completely cured. Pesme found it possible to distinguish, from the location of the blood vessels, between corneal syphilis and corneal tuberculosis. According to Vogt the deep-lying vessels mainly ran close to Descemet's membrane, nearly all of them at the same level. The horizontal vessels often proceeded at direct angles to the vertical ones. The vessels sometimes followed the course of nerves. Berliner, likewise, considered the location of the deep blood vessels near Descemet's membrane characteristic of the disease.

Corneal vascularization in the active phase of the disease has usually been regarded as a kind of crisis in its course and as a first sign of the commencement of recovery. Their appearance has been interpreted as a protective measure of the organism and as a circumstance which promotes the clarification of the cornea. Herzau and Hossmann declared, however, that they had noted development of deep blood vessels in the cornea before the appearance of any other corneal haziness. Deep blood vessels, on the other hand, in themselves have an impairing effect on vision, and in some cases they possibly obscure their surroundings by furthering fibrosis. In some of my own cases I noted, in fact, a dense, sheet-like opacity, on a level with and around the blood vessels proceeding near Descemet's membrane.

The deep blood vessels have usually been supposed to be permanent (v. Hippel, Berliner), either as such or after having become obliterated. In the latter instance, however, the vascular lumina may reopen, if there is a recurrence or a process that increases corneal metabolism. v. Hippel considered the vascular and avascular forms different stages of the same disease. Several investigators (Trousseau, Cosmettatos, Igersheimer) found slight vascularization or its entire absence characteristic of interstitial keratitis due to acquired syphilis, although Igersheimer called in question whether acquired syphilis alone could give rise to typical interstitial keratitis.

Among the 178 corneas which I examined with a slit lamp I did not note a single one with only obliterated blood vessels. Instead, a thinner branch of a larger and open vessel might quite often be closed. In some of the blood vessels, in fact, the lumen was so small that the red cells could not circulate even in a one cell wide successive chain, but only now and then one cell at a time passed through the lumen.

I did not note any settling down of the blood vessels in the parenchyma at a definite level, but one met them at all depths. It was usual for more superficial and deeper vessels to anastomose. Large trunk vessels were common and they proceeded nearer to the corneal periphery, following the limbus. I did not come upon any single brush-like form typical of the active phase of the disease. As a rule the process of vascularization seemed to concentrate itself to the marginal parts of the cornea, but thin vessels nevertheless passed on as far as the centre. No subepithelial, pannus-like system of blood vessels occurred in my material.

In one of my cases (Case Rec. 346/49), which I was able to observe from the beginning of the active phase, the disease set in with iridocyclitic symptoms: the iris was hyperaemic, there was an abundance of precipitates, and the corneal parenchyma was evenly opaque. In this case no deep vessels appeared in the cornea until the termination of the retrogressional phase of the disease, when the deep

infiltrations which had later on formed in the cornea and other symptoms were already disappearing. The disease ran a relatively benign course so that the slight vascularization, in this case, supported the widely accepted view that the keratitis when more avascular was less severe. Herzau and Hossmann's and my own case seem to show that the progress of vascularization, when occurring in the cornea, is not bound up with a definite phase of the disease but is only dependent on the metabolic conditions of the cornea, which is in good agreement with v. Hippel's view of the nature of vascularization. It is also supported by the following interesting observation I made. A 15-year-old patient had developed interstitial keratitis in the left eye. 7 years later I noticed deep blood vessels in the left cornea, along with scars. On the other hand, the keratitis which developed 7 years later in the right eye, did not cause any vascularization within 1 year of observation, after the active phase of the disease.

This case alone shows that *there is hardly any justification for making a distinction between different forms of interstitial keratitis on the basis of the vascularization noted*. If we stick to the view that deep vascularization is something permanent, either with open or obliterated vessels, then in about 15 % of the cases in my material the keratitis was of an avascular type. This is a considerable percentage if one considers absence of vascularization to some extent typical of interstitial keratitis due to acquired syphilis. All my own patients, as I have said, could be proved to suffer from congenital syphilis.

When estimating deep vessels I considered as such only those that belonged to a vascular system projecting several millimeters into the cornea from the limbal network. The following Table records my observations about the frequency of deep blood vessels compared with the figures of Herzau and Hossmann and Dalsgaard-Nielsen (Table 14, p. 83).

The Table may be summarized as speaking for the permanence of deep blood vessels, especially if my figures and those of Dalsgaard-Nielsen are compared with the values

TABLE 14

Occurrence of deep vessels in the cornea, in Herzau & Hossmann's, Dalsgaard-Nielsen's and the author's material

	Herzau & Hossmann's 433 cases	Dalsgaard- Nielsen's 214 corneas	Author's 178 corneas
Deep vessels in cornea	95,8 %	88 %	84,8 %
Corneas of avascular type	6,2 %	12 %	15,2 %

obtained by Herzau and Hossmann in the active phase.

Can the age at which the patients developed the disease possibly have some share in the formation of deep blood vessels? To find out about this I divided those of my cases which were of avascular type into different groups on the basis of the age when the disease appeared. I then obtained the following figures: 3 cases at 1—5 years of age, 3 cases at 6—10, 3 between 11 and 15 years, 12 between 16 and 20, 5 cases between 21 and 25 and 1 case at 30 years of age. From the distribution of the patients among the different years of involvement one might suppose, in spite of the smallness of the material, that although avascular keratitis occurs in all the age groups yet it is more frequent among patients who developed the disease at an older age than the average, which may perhaps be taken as a sign of increasing resistance of the organism with age.

c. Changes in the Descemet's Membrane and the Endothelium

In contrast to findings in the endothelium the pathological changes in *Descemet's membrane* are relatively slight both during the disease and after (v. Hippel, Elschmig, Watanabe, Seefelder, Bentele). Gilbert noted thinning of Descemet's membrane where the scars were, and Kunze saw, for example, disintegra-

tion of tissue, defects and vagueness of structure in places, yet nowhere infiltration. Several investigators have observed that parenchymal infiltration often involves tissue as far as Descemet's membrane but no farther (Watanabe, Kunze, Igersheimer, Seefelder et al.). Even ruptures have been noted in Descemet's membrane (v. Hippel).

Both Vogt and Berliner, in their biomicroscopy text-books, considered opacity of Descemet's membrane and the appearance of deep vessels in its neighbourhood characteristic of the sequel of interstitial keratitis. Vogt made a distinction between different kinds of opaque surfaces in Descemet's membrane. They were whitish, translucent, their edges were often concave, and they sometimes contained roundish clear holes. According to Berliner, a rupture of Descemet's membrane could cause concentric, ring-like opacities in interstitial keratitis, especially in Vossius' annular type of the disease. v. Hoyer attributed the folds appearing in Descemet's membrane to variation in tension, and he presumed that the concentric, pericentral folds he saw were associated with the granulating central exudate network of the posterior surface of the cornea. Igersheimer did not believe that variation in tension had any share in the process of folding. According to Vogt the folds in Descemet's membrane were indicative of a severe corneal disease, and they were associated with changes in tension, mainly hypotonia. Granström noted folds in the Descemet's membrane of 6 out of 7 patients who had developed the disease at over 30 years of age, and he thought that the appearance of the folds was due to reduction of corneal elasticity along with age. Berliner believed that they resulted from variations in tension, corneal oedema and scars.

In my own material I encountered *folding of Descemet's membrane* in 13 out of 178 corneas, or 7.3%. 8 of them were bilateral. In 12 corneas the folds formed a ring, in 1 they ran radially. Schweickhardt noted folds of Descemet's membrane in 1.9% of 148 eyes, and Dalsgaard-Nielsen in 2% of 214. The folds were thus

more frequent among my own patients, which circumstance, according to V o g t, would witness to my cases being of a severe type. L e h m a n n found folds in as many as 17 % of his cases, but this figure covered also the hyaline striae on the posterior surface of the cornea.

To estimate the part played by the age at which the disease first appeared, in the folding of Descemet's membrane, I divided my cases into groups on the basis of the age of the onset of the disease. I obtained the following classification: 6 corneas between 11 and 15 years, 5 corneas between 16 and 20, 2 corneas at 21—25 years. This hardly justifies generalizing G r a n s t r ö m's conception about the significance of the age at which the disease sets in, in the appearance of the folds. Folds were comparatively more frequent in the older age groups in my material, but there were none in patients who developed the disease at over 30, in whom G r a n s t r ö m found them especially often. And below 20 years one can hardly speak of reduction in elasticity because of age.

Sheet-like opacity of Descemet's membrane, which V o g t and B e r l i n e r considered characteristic of interstitial keratitis, specifically, I noted in 8 eyes among my material, or 4.5 per cent. I find the change typical of the disease though not very common. In many cases it is difficult to obtain a view of it because of parenchymal opacities. I did not find that the age at which the disease appeared had any clear effect on the development of the symptom. In contrast to folds, its incidence is somewhat larger in the younger age groups.

Changes are thus not very common in Descemet's membrane, and considering the usual site of the infiltrations and the deep blood vessels in the deep parenchymal layers, and the manifold endothelial changes, they are surprisingly rare. In this respect Bowman's and Descemet's membrane react in the same way.

Most investigators have noted great patho-anatomical changes in the *endothelium* both in the active phase and in old cases. The endothelium could be entirely lacking, and the cells had changed both in form and structure. K u n z e,

conversely, held that there were relatively few pathological changes in the endothelium. Many authors have paid especial notice to the deposits on the posterior surface of the cornea, and there are very different views about their character. v. Hippel and Gilbert noted, on the back surface of the cornea, a deposit consisting of connective tissue which bulged into the anterior chamber. Igersheimer believed they were primary formations caused by a spirochete — in animal experiments he could see spirochetes in them — while Seefelder, for instance, agreed with Elschnig in considering them only secondary formations. Igersheimer divided the deposits on the posterior surface into endothelial cell clumps and formations of inflammatory origin, in which for instance lymphocytes, leukocytes, giant cells and fibrin might occur. Precipitates, inflammatory in character, were very common in the active phase, less frequent in conditions following the disease, and occurred then mainly in the form of pigment precipitates. Vogt, with a slit lamp, noted on the endothelium after interstitial keratitis crater-like formations, mainly where there were scars. Vogt supposed that substances (toxins), carried in the deep blood vessels, could act as predisposing agents to the formation of precipitates.

After interstitial keratitis one may encounter, on the posterior surface of the cornea, partly protruding into the anterior chamber, ribbon-like formations, often ramifying, of which designations such as »Glashautleisten» and »hyaline striae» have been used in the literature. When describing 3 cases in which interstitial keratitis had occurred 3, 10 and 50 years ago, Stähli explained these formations as consequences of the cicatricial contraction of the cornea. Weill and Jost considered these ribbons endothelial formations which were caused by severe interstitial keratitis and greatly resembled the ruptures of Descemet's membrane occurring in buphthalmos. Kestenbaum described one case in which the ribbon stretched from the cornea as far as the iris. The author supposed that it was formed by the organized exudate of the anterior chamber. Vogt measured the widths of the ribbons as 0.2—0.3 mm. He

believed they were actual deposits on the posterior surface of the cornea, formed of the fibrin of the anterior chamber. According to V o g t the shape of the ribbons varied a good deal, they could sometimes even form stars. As a rule their edges were distinct, but in one of his cases V o g t saw the end of the ribbon dissolving into the aqueous humour without any distinct border.

In my own material I almost regularly noted slight unevenness in the posterior surface of the cornea, but, with the slit lamp, no actual protuberance in any single case. In many cases, it was difficult to estimate the posterior surface of the cornea because of the opacities, so that there is hardly sufficient justification for bringing out more exact figures for slight endothelial changes. Actual precipitates, on the other hand, were more easily discernible. In my own cases I saw only dark, so-called pigment precipitates in 16 eyes, or 8.9 %. D a l s g a a r d - N i e l s e n noted precipitates in 8 % of his cases. In one cornea (Case Rec. 296/45) I found the pigment precipitate taking on a very specific form, that of a pigment ring, $1\frac{1}{2}$ in diameter, in the centre of which the cornea was quite clear. I noted hyaline striae in only 2 eyes, or 1.1 %. In both these cases the ribbon ramified and a part of it passed on as far as the anterior chamber. Neither of my cases was severer than usual.

Thus I was able to note *clear endothelial changes* in 10 % only of my cases, which figure is evidently lower than their real number, for, as I said, in many cases it is difficult, even impossible, to estimate the endothelium.

In my material the number of corneas in which no pathological changes could be seen after 8 years on an average was 8, or 4.5 %, which is contributory evidence of the fact that interstitial keratitis almost regularly brings about, through corneal changes, considerable or slight impairment of vision.

2. *Changes in the Chamber Angle*

Patho-anatomical changes of the chamber angle occur often in both fresh and old cases of interstitial keratitis. Elsch nig, Jaeger, Seefelder and Bentele et al. noted in their fresh cases in the tract of ligamentum pectinatum infiltration of round cells and leukocytes, involving tissue as far as corpus ciliare. Other authors found in their old cases closing of the chamber angle (v. Hippel), synechiae, infiltration and pigmentation (Kunze). J. S. Friedenwald made a patho-anatomical study of infants with congenital syphilis and noted, for example, infiltration in the chamber angle. Yokota presumed that the spirochetes giving rise to interstitial keratitis invaded the cornea from the direction of the chamber angle, and the first changes would thus be observable in the tract of the ligamentum pectinatum.

Because of corneal opacities I was able to see the chamber angle in only 17 eyes, which I examined with Goldmann's gonioscopy lens and the slit lamp. Changes were then revealed in 13 eyes. Ciliary and trabecular synechiae were present in all, occurring in abundance all along the chamber angle, of which the single synechiae, however, were rather narrow, about 1—3 mm. Increased pigmentation occurred, besides, in the tract of the ciliary body of 15 eyes. I did not notice any correlation between the corneal opacities and the changes in the chamber angle.

I have not found any gonioscopic studies of the chamber angle of patients with interstitial keratitis in the literature, so that comparison is impossible. *The great number of the changes in the chamber angle*, in spite of the relative meagreness of my material, *speaks for uveitis being associated with the active phase of the disease*. In 8 out of the 13 eyes in which I found changes in the chamber angle, vision varied between 1.25—0.5. My observations do not support Igersheimer's theory that there is simultaneous iritis in 50 % of cases of interstitial keratitis. There are others, for instance Cattaneo, Seefelder and de Sanctis, who hold that every case of interstitial keratitis is accompanied by iritis.

3. *Changes in the Iris*

Hutchinson was among the first who declared that infantile syphilitic iritis is much more common in congenital syphilis than has usually been supposed. Because of the often slight symptoms the disease remains unidentified. Hutchinson reported on 23 cases which he had studied, in which the average age was 5—6 months and in 12 of which a pseudomembrane developed in the pupil. Igersheimer, again, considered iritis a comparatively rare condition in the congenital syphilis of infants. J. S. Friedenwald wrote on the basis of his investigations that iridocyclitis occurred quite often in cases of congenital infantile syphilis.

Those authors who proceeded patho-anatomically regularly found in cases of interstitial keratitis, both in the active phase and in older cases, iridial infiltration containing large, vesicle-formed, anuclear cells, cells rich in protoplasm, lymphocytes, leukocytes, eosinophil and giant cells, and others. Both infiltration and hyalinization had often occurred around the blood vessels. Disintegration of the pigments of the posterior pigmented iris layer and the stroma had been of almost regular occurrence. In the stroma, hyalin degeneration and atrophy of muscular tissue had been noted (Gilbert).

For the rest, very few studies of other changes in the iris associated with interstitial keratitis have been founded on at all adequate material. There are several reasons to account for this. Among the most important, it would seem, is the fact that the iris is usually poorly visible because of the corneal scars, and the difficult appraisal of iridial changes. Senile and post-inflammatory changes of the iris are often so much alike that it may be difficult, even impossible, to make any distinction between the two types in older patients. The results are easily too much conditioned by subjective factors, such as the familiarity of the investigator with his subject, technique of the investigation etc. Though aware of the these difficulties I have yet attempted to find out about the changes in the iris appearing after interstitial

keratitis. I restricted my studies to only some of the most important and most easily estimable changes.

Atrophic changes in the iris are due both to degeneration of the posterior pigmented layer and changes in the stroma. In my own studies I looked for pigmentary degeneration by the technique which Vannas used in his extensive clinical and experimental investigations and which other authors have since then found serviceable for establishing even slight pigmentary defects. Accordingly, I distinguished as a separate group the eyes in which I noted depigmentation of the posterior pigmented iris layer by retroillumination. It appeared in the form of lesser optical density or even as illuminated patches in the iris. In these cases there were simultaneous atrophic changes in the stroma, which facilitated the detection of depigmented areas. The areas I noted were fairly large, about 2—3 mm in diameter, and mainly occurred in the part of the iris nearest to the pupil.

The other group consisted of irides in which the pigmentary degeneration had taken the form of disintegration, i.e. as small dark particles of pigment which had gathered on the surface of the iris. The symptom might be compared with a kind of scattering of soot down onto the iris. I took into account only the cases in which there was an abundance of pigment particles covering at least half of the irideal surface.

I put down a stroma as atrophic if it appeared thin and veil-like in consistency and presented an even surface so that the difference in height between the pupillary and ciliary part was levelled. The trabeculae, at the same time, stretched in thread-like formations, as it were, radially, so that the crypts disappeared almost totally. Here and there the blood vessels stood out in more relief as reddish, faint thin threads, proceeding mainly radially. I was also on the look-out for possible dilated so-called varicose veins, besides.

I also looked for posterior synechiae and organized exudate of the iris in my cases. My findings do not give a quite correct picture of these cases because of the dis-

advantage of my not being able, for practical reasons, to use media dilating the pupil. Further, I tried to look for possible ectropium of the posterior pigmented iris layer.

I examined 128 irides in all, in 10 of which, or 7.8 %, optically establishable holes occurred in the posterior pigmented layer. In all these cases there were atrophic changes in the stroma, of the kind described in the foregoing. In 12 eyes, or 9.4 %, I noted dark pigment particles on the surface of the iris. Atrophy of the stroma without any changes in the posterior pigmented layer occurred in 26 eyes, or 20.3 %. I saw posterior synechiae in 9 eyes, or 7 %, and organized exudate of the irideal margin in 2 eyes, or 1.6 %. Ectropium of the posterior pigmented layer of the iris I noted in 5 eyes, or 3.9 %. A varicose blood vessel was disclosed in only 1 iris. I did not note a single instance of heterochromia.

Changes in the stroma and the posterior pigmented iris layer that could be put down as atrophic occurred in 53 irides altogether, or 41.4 %, which figure is considerably larger than any I have met in the literature. Dalsgaard-Nielsen noted atrophy of the iris in 2 % only, while there were synechiae in 14 %.

To judge from Hutchinson's and Friedenwald's observations, iritis developing as early as infancy could be followed by atrophic changes in the iris. In some of my cases, perhaps, the iridial changes may be attributed with more justice to the said iritis than to later interstitial keratitis. The statements of many investigators, that interstitial keratitis is always accompanied by iritis, and pathological investigations almost make it inevitable that the changes in the iris, as well, should often be permanent. This is borne out clearly by my own observations related in the foregoing. My findings are also in good accord with what I noted about the frequency of changes in the chamber angle. It would indeed be almost surprising if, since there are such considerable changes in the cornea and fairly common changes in the eye fundi, signs of the disease would occur only seldom in the iris.

A circumstance which would deserve more notice than

has been given to it so far is the clearing up of the question of the interrelation between infantile iritis and interstitial keratitis. Heine believed that most cases of interstitial keratitis developed from primary iridocyclitis. In my own material some data, though only anamnestic, which I got from 2 patients, seem to show that they very probably had developed a disease resembling iritis in early infancy. 3 other patients, besides, had manifested an eye disease of the same kind between 2 and 4 years of age.

4. *Changes in the Lens*

In the lens the changes take the form of pigmentation of the surface and cataract formation. Both changes are secondary and in no way typical. In various patho-anatomical examinations the lens has usually been found symptomless.

Green examined 100 children under 14 years of age suffering from congenital syphilis and noted a posterior polar cataract in one. Carvill and Derby found opacity of the lens in 7 eyes out of 362, or in 1.9 %, but of these cases 1 was traumatic. Dalsgaard-Nielsen noted opacity in 5 % out of 183 cases, which he supposed had been caused by interstitial keratitis. Pigment particles were seen on the surface of the lens in 8 cases, or 4 %. Of McLeod and Lemoine's 60 patients with interstitial keratitis only 2 had a cataract.

In my own material I noted opacity of the lens which was unmistakably connected with the disease in 1 eye (Case Rec. 784/31) only, or 0.8 %. It was a central one, in the anterior capsule. In most of my cases corneal opacities prevented, to some extent, a clear view of the lens, so that the figure I obtained is obviously too small. Yet my findings show that the opacity of the lens is not a very important factor among those causing deterioration of vision in cases of interstitial keratitis. I noted dark pigment particles on the surface of the lens in 8 eyes, or 4.5 %, which finding corresponds approximately to what I saw about pigmenta-

tion on the posterior surface of the cornea and the surface of the iris.

In the vitreous, where secondary changes are said to occur sometimes, I did not notice anything out of the normal in any of my patients.

5. *Changes in the Choroid and the Retina*

H a a b classified the changes in the eye fundus into the following types: (1) »Pepper and Salt» fundus, (2) large pigmentary patches in the fundal periphery and (3) mainly white patches in the fundal periphery. Sidler-Huguenin, again, distinguished between the following 4 types: (1) »Pepper and Salt» fundus, (2) largish, mainly pigmentary patches in the fundal periphery, (3) largish, mainly whitish patches in the periphery, and (4) a clinical picture resembling that of retinal pigmentary atrophy. Sidler-Huguenin noted in his own material consisting of 125 patients with congenital syphilis changes of the eye fundus which distributed themselves as follows: Type 1, 30 cases (24 %), type 2, 47 cases (37.6 %), type 3, 23 cases (18.4 %), and type 4, 21 cases (16.8 %). The great number of the fundal changes classifiable as type 4, which Sidler-Huguenin mentions, is noteworthy. He declared that type 4 was characterized by a change of the colour of the eye fundus to a more leadish grey. The author did not think there could be any shift from one type to another, and he considered each of them conditions distinct from interstitial keratitis. In not a single one of his cases did he find that the fundal changes had developed after interstitial keratitis. In the first type the changes were retinal, in the second both retinal and choroidal, yet more of the former kind, the third type was again choroidal and in the fourth the disease affected the pigmented epithelium. Sidler-Huguenin attributed the disease to patho-anatomical changes in the long and short posterior ciliary arteries and the anterior ciliary arteries. All the changes

persisten through life, and the prognosis was relatively good. The changes in the eye fundus were both inflammatory in nature and also, as a result from vascular alteration in the choroid, degenerative.

Carvill and Derby described 2 remarkable changes of the eye fundus. In one there was increased pigmentation in the neighbourhood of the macula and in the other a white patch surrounded by pigment particles in the macula and arteria hyaloidea persistens at the same time. Igersheimer did not consider chorioretinitis a constituent in a typical clinical picture of interstitial keratitis. They were connected with each other only through the circumstance that spirochetes entered both tissues simultaneously, while the uvea usually became involved much earlier. As a rule the outbreak of keratitis was not conditioned by inflammation of the uveal tract, although the patients who had typical peripheric chorioretinal patches were in some way predisposed to interstitial keratitis. Chorioretinitis often occurred as early as infancy. According to Igersheimer type 2 was the most common and type 3 very rare. Central chorioretinitis, also, appeared in congenital syphilis, and one form of it was known under the name chorioiditis circum-papillaris. Igersheimer believed that spirochetes entered the eye by way of blood vessels and affected the choroid but also the retina directly or through toxins. The spirochetes might pass on to the walls and the neighbourhood of vessels causing, through nutritional disturbance, secondary changes especially in the retina.

J. S. Friedenwald classified the changes of the eye fundus into the following types: (1) chorioretinitis circumscripta, which is very atypical, (2) »Pepper and Salt» form, which is typical of congenital syphilis and may develop into a fundal condition simulating pigmentary atrophy of the retina, (3) a fundal change characterized by retinal scars, vascular atresia and atrophy of the optic nerve, all of them occurring at the same time, and (4) a disease of the eye fundus resembling pigmentary atrophy of the retina, which, besides developing from the »Pepper and Salt» type, may also set in independently. Colomba (1936) noted

changes of the fundus after interstitial keratitis in 19 out of his 29 patients, of whom 27 suffered from congenital syphilis.

Most patho-anatomical studies mention changes in the choroid and the retina, and spirochetes have been found in them as well. Choroidal and retinal infiltration belong to the commonest changes. Adherences occur now and then in some parts of the choroid and retina as well as absence of Bruch's membrane (v. Hippel). v. Hippel, Gilbert and Kunze et al. noted atrophy of the pigment epithelium, the rods and cones, nuclear layers and the ganglion cell layers. The pigment had dispersed from the pigment epithelium into the adjacent tissue, usually into the inner retinal layers. Along with the atrophic areas, cicatricial tissue starting from the choroid adds to the thickness of the choroid and the retina in places. There are other typical changes, besides, in the blood vessels, where one meets with perivascular infiltration and increase of leukocytes in the lumina (v. Hippel).

In my own material I examined 185 eye fundi, most of them, it is true, without mydriatics. The picture of the eye fundus lacks accuracy even in otherwise thorough examinations if the pupil is not dilated, but I am nevertheless inclined to believe that the differences are not so large as to be of any decisive value. In all these cases the interstitial keratitis was bilateral. 9 of my patients with eye fundus changes could be put down as Sidler-Huguenin's types 1 and 10 as types 2. None of the eye fundi were classifiable as types 3 or 4. In only 1 eye of the 19 a disease of the eye fundus, obviously of type 2, seemed to have an impairing effect on central vision. In the other 5 cases the picture of the eye fundus deviated so much from the rest both as regards the nature of the patch and its site that I distinguished them as separate groups. In all these cases I noted in the region of the macula a patch the size of $\frac{1}{2}$ —1 papilla, with distinct borders, whitish, partly or totally surrounded by a pigment ring, which in my cases obviously affected the patients' sight. Everywhere else the eye fundi had a normal appearance. A more frequent occurrence of this macular patch than was expected; the physiolo-

gical and anatomical specific features in the macular region and the lowered vision noted in connection with the change seemed to speak for the classification I made. In all these cases the patch was unilateral, the other eye fundus being quite normal.

In Table 15 (p. 96) I made a comparison between the incidence of chorioretinitis in cases of interstitial keratitis and congenital syphilis as recorded in the literature and my own results.

TABLE 15

Occurrence of chorioretinitis in association with congenital syphilis and interstitial keratitis in some other investigators' and the author's material

Cunningham	White & Veeder	Carvill & Derby	Herzau & Hossmann	Schweickhardt	Hoehe	McLeod & Lemoine	Klauder & Vandoren	Authors' material
68 %	3,3 %	68 %	5,5 %	25 %	28 %	36,6 %	7,9 %	12,1 %

White and Veeder's and McLeod and Lemoine's results were obtained by examining patients with congenital syphilis who had not developed keratitis. White and Veeder's patients were all cases of late congenital syphilis.

In Table 16 (p. 97) I have compared my findings with those of some other authors on the basis of Sidler-Huguenin's differentiation. Unfortunately I found, in the literature, only few studies of eye fundi based on this classification.

The figures recorded show large differences, all of which can hardly be accounted for by the different techniques of investigations used by the authors, the conditions in which or the skill with which the investigations were carried out. The differences are especially striking in a comparison of the figures of the Americans McLeod & Lemoine and White & Veeder and those of Carvill & Derby and Klauder & Vandoren. What the differences are due to we do not know, but one might

TABLE 16

Occurrence of Sidler-Huguenin's types of eye fundus in some investigators' and the author's material

Siedler-Huguenin's type	Nordmann's patients with interst. kerat.	Dalsgaard-Nielsen's patients with interst. kerat.	Author's material
1	13,3 %	1 %	4,8 %
2	15,5 %	} 14,0 %	5,4 %
3	—		—
4	—	1 %	—

suppose that local and even temporal variations occurring among the patients with interstitial keratitis may contribute to them. If it were possible to make a patho-anatomical study of all these cases, the figures might change considerably. There is indication of this in the results of well-known histological investigations. Apparently only a small part of the patho-anatomical changes stand out clinically. The individual and racial differences in the pigment matter may also play some part. My own values are in approximate agreement with those obtained by Dalsgaard-Nielsen in Denmark and, because of my technique, are very likely somewhat lower than the actual ones.

6. Changes in the Optic Nerve

In most patho-anatomical examinations the optic nerve has appeared intact. v. Hippel mentions, nevertheless, that he had noted increase of cells in the papilla and the optic nerve. J. S. Friedenwald found changes in the optic nerves of 2 of his patients: disorganization of the optic nerve so that the fibre sheath became indistinguishable, proliferation of glial tissue and infiltration of myeloid cells, and new vascularization.

Changes have been revealed in the optic nerve clinically as well. Heine noted primary inflammation of the optic nerve of as many as 81.9 % of 105 infants affected with congenital syphilis. Not nearly all of the other investigators obtained as high a figure as this. Igersheimer considered both papillitis and atrophy of the optic nerve rare in congenital syphilitic infants. Cole, Usilton, Moore et collab. noted atrophy of the optic nerve in 2.5 % among 1010 patients with congenital syphilis. McLeod and Lemoine examined 208 congenital syphilitic eye fundi, in which primary atrophy of the optic nerve occurred in 5 cases, or 2.4 %, and secondary in 22, or 10.6 %.

In older patients with congenital syphilis, i.e. when there is interstitial keratitis as well, changes of the optic nerve are found to be relatively rare. The incidence of atrophy of the optic nerve is illustrated for instance by the following figures: Carvill & Derby 2.5 %, Herzau & Hossmann 0.7 %, Saul 1.0 % and Schweickhardt 4.6 %. Schweickhardt noted, besides, inflammation of the optic nerve in 3.7 % of his cases.

In my own series of patients I examined 185 eye fundi. I saw changes in the optic nerve of 2 patients only, in 4 eyes altogether, or 2.2 %. The optic nerve was atrophied in all these eyes. In view of Heine's figures one might have expected a much larger incidence of atrophy of the optic nerve among older congenital syphilis patients. My findings seem to confirm the concept that *atrophy of the optic nerve has only little share in the impairment of vision in cases of interstitial keratitis and in congenital syphilis in general.*

Summary

For this study the fresh cases of interstitial keratitis associated with congenital syphilis occurring in Finland in 1922—50 were brought together from the materials of different Eye Departments. In 128 cases out of these I carried out many different kinds of follow-up examinations personally, on an average 8 years after the active phase of the disease. The mean age of the follow-up patients was then 23 years.

1100 fresh cases, approximately, of interstitial keratitis associated with congenital syphilis occurred in Finland in 1922—50. *There has been no appreciable decline in the incidence of the disease within this time.* The number of cases in the whole country is probably about 2000—2200 at present.

58 % of the patients developed the disease between 4 and 12 years of age, and 31 % between 13 and 22.

Regardless of the greater number of female patients with congenital syphilis noted in Finland, there is no marked female preponderance among the patients affected with interstitial keratitis.

Only 9.4 % of 126 patients lacked so-called *congenital-syphilitic signs* (except keratitis). Only one patient of 126 had clear endocrine disturbances.

On the *blood* the Wassermann, cholWassermann or Kahn tests were positive for 48 out of 109 patients, or about 44%. Out of 82 patients who received specifically appropriate treatment 48 % responded positively to the reactions or some of them and only 9 of the 27 patients who had been given slight treatment or none. For more than a half of the serologically positive patients only the Kahn reaction was positive.

The *liquor* of 40 patients was examined and pathological changes were noted in only 2 cases. Only one patient had clinical neuro-syphilis.

Anamnestic information was available of the *family conditions* of 117 patients born in marriage. There were 4 pregnancies on an average to each of these families. Infant mortality was 5.2 %. In only 29 families had either one or both parents been examined to ascertain syphilis. The blood reaction was positive for the mother in 92.9 % and for the father in 45 % of the cases. Judging from the blood reactions of my patients and their brothers and sisters only about every 5th child born in marriages of syphilitic parents would develop congenital syphilis which could be established serologically. According to my results only about 1/4 of the family members of the now living patients with interstitial keratitis had been examined for syphilis. The past history of the patients showed that only 3 of their brothers and sisters had developed interstitial keratitis.

The bulk of my patients affected with interstitial keratitis associated with congenital syphilis were acceptable and useful members of society. 73 of the patients who were followed up had acquired a higher *social status*, on an average, than that of their parents.

The vision of 126 patients (224 eyes) was examined in the follow-ups. The following result was obtained when only the better eye was taken into account: Excellent vision in 30.6 %, good vision in 37.9 %, fair vision in 22.6 %, poor vision in 5.6 %, counting of fingers in 2.4 % and blind in 0.8 % of the cases. There was no appreciable difference in this respect between those who had received specifically vigorous treatment and those who had been treated slightly or not all. In 9 only out of 178 eyes was the bad vision due to some other reason than corneal opacities.

Only slight *disability* was brought about by the disease in most of the cases. 70 % of the patients were 0—5 % invalids, of whom 18.4 % of the 5 % degree. Thus slightly over one half of my patients had retained full capacity for work as far as vision was concerned.

Of *refractional changes* myopia occurred in 33 %, hyperopia

in 8.1 %, and astigmatism in 37 % of the cases. A higher degree of myopia (over 6 dioptries) seemed to be connected with an early age of involvement.

Recurrence occurred in 12.5 % of my cases.

Bilateral involvement of the eyes was noted within 1 year from the outbreak of the disease in the first eye in 92.7 % of the cases and within 2 years in 95.4 %. The interval was over 5 years in only 3.7 % of the bilateral cases. The amount of the antisyphilitic treatment and the lapse of time between the involvement of the two eyes, and between the antisyphilitic treatment given in the interval of the two involvements and the ultimate vision of the eye involved later were not interrelated. Present antisyphilitic methods of treatment did not seem to have any effect on the outbreak of the disease, its course and recurrence, at least not when given in late congenital syphilis.

In follow-ups the *corneal sensitivity* was examined with 3 different so-called Frey's hairs. Clearly reduced corneal sensitivity was noted in only one out of 71 corneas. Corneal sensitivity that had remained normal after interstitial keratitis was some kind of evidence of the relatively good preservation of the metabolism of the cornea and especially its epithelium. This perhaps provides one explanation for the often surprisingly good recovery of the eye after a severe inflammatory condition. Possibly we have here something to account for the comparatively good operative results obtained by corneal transplantation on patients affected with interstitial keratitis.

Of *other eye changes*, concomitant strabismus occurred in 13 patients, or 10.2 %, in 10 of whom it was of the divergent type. Three patients had paralytic strabismus: in 1 case n. trochlearis was paralyzed and in 2 n. abducens. Pupillary changes occurred in 11 patients, or 8.8 %, ptosis in 3 and nystagmus in 1. One patient manifested night-blindness. The tension of 2 patients had risen and of 3 fallen. I considered the sclera atrophic in about 1/4 of my cases.

Biomicroscopic follow-up examinations were carried out on 178 corneas. Vogt's white limbus girdle was then seen

in the epithelium and the tract of Bowman's membrane of one patient and a change resembling C o a t s's white rings in another. A pigmented line was revealed in 16 corneas, or 8.9 %. These changes, obviously, are indicative of degeneration or inferiority of the corneal tissue in question.

Parenchymal scars were noted in 95.5 % of the cases. The scar was patch-like in 54.5 %, smoke-like in 37.1 % and a leukoma in 3.9 %.

The *deep blood vessels* of the parenchyma are very important for diagnosis, afterwards. Deep vessels occurred in 84.2 % of the cases. My findings speak for the permanent character of these blood vessels, either in an open or an obliterated condition.

Folds were observed in the *Descemet's membrane* of 13 eyes, or 7.3 %. There seemed to be probable causality between hypotonia and the folds. Changes of the endothelium occurred in about 10 % of the cases.

An examination of the *chamber angle* with a gonioscopic lens revealed changes in 13 out of 17 eyes, which finding seems to imply that iritis is a fairly common co-existent condition in the active phase.

Atrophic changes of the *iris* (in the stroma and the posterior pigmented layer) occurred in 53 eyes, or 41.4 %.

Changes of the *eye fundus* due to congenital syphilis were revealed in 24 eyes, or 12.1 %.

Numbers of the Case Records or the Cards of Follow-up Cases

For practical reasons I have inserted in the text the case records of only some of my most interesting cases. The numbers of the case records or the cards of all my follow-up cases, replaced, in the absence of numbers, by the initials of the patients' names, appear in the following list. Full reports are available in the files of corresponding Eye Departments.

The Ophthalmic Clinic of the University, Helsinki, 39 patients, the numbers of whose case records are: 540/24, 577/25, 248/26, 513/26, 174/27, 141/29, 269/29, 674/30, 1045/30, 372/31, 784/31, 865/31, 699/32, 42/34, 451/36, 73/37, 135/37, 121/39, 370/39, 1213/43, 120/44, 1058/44, 229/45, 594/45, 232/46, 1080/47, 401/48 and 738/48, and the numbers of out-patients' cards are: 5334/25, 4261/26, 551/27, 8310/27, 3050/37, 4123/37, 3477/38, 4400/41, 4589/41, 1440/42 and 5695/47.

The Ophthalmic Clinic of the University, Turku, 26 patients, the numbers of whose case records are: 72/40, 216/41, 151/42, 49/44, 52/44, 63/45, 111/45, 216/45, 296/45, 313/45, 96/47, 178/48, 469/48, 524/48, 184/49, 207/49, 346/49, 302/50 and 330/50, and whose out-patients' cards, initials standing for their names, are: I.L./47, M.S./47, S.A./48, L.P./48, N.V./48, P.V./48 and E.N./50.

The Ophthalmic Department of Diakonissakoti Hospital, Oulu, 35 patients, the numbers of whose case records are: 1038/32, 376/33, 204/34, 1861/34, 1207/35, 2328/35, 981/37, 1508/38, 1703/38, 1189/39, 1455/39, 1839/40, 1796/40, 2148/40, 2434/40, 352/41, 1574/41 and 827/42, and whose out-patients' cards, initials standing for their names, are:

J.L./43, K.E./44, J.A./46, E.E./47, R.H./47, H.J./47, R.K./47, V.K./47, S.M./47, T.T./47, T-i.V./47, T-o.V./47, S.Y./47, E.B./48, E.K./48, P.K./48 and S.S./48.

The Ophthalmic Department of Diakonissalaitos Hospital, Lahti, 16 patients, the numbers of whose case records are: 100/41, 222/41, 178/42, 296/42, 312/42, 1/44, 377/45, 18/46, 151/46, 200/46, 332/46, 424/46, 112/47, 158/48 and 491/48, and out-patients' card, initials standing for name, L.K./44.

The Ophthalmic Department of Kivelä Hospital, Helsinki, 6 patients, the numbers of whose case records are: 78/38, 15/41, 206/42, 3/45, 145/45 and 378/48.

Kumpula State Hospital for Venereal Disease, Helsinki, 6 patients, the numbers of whose case records are: 562/48, 750/48, 437/49, 537/49, 931/49 and 934/49.

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